



SECOND EDITION

COMPARATIVE VERTEBRATE NEUROANATOMY

Evolution and Adaptation

ANN B. BUTLER / WILLIAM HODOS

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Evolution and Adaptation

Second Edition

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College Park, Maryland

 **WILEY-
INTERSCIENCE**

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Dedication

This dedication is in four parts: to those special friends, mentors, and family members who are now deceased, to those special persons still living who have taught and guided us in our careers, to a special friend of the field, and to our families.

In recognition of those special persons who are now deceased, Ann Butler dedicates her contribution to this work to the memory of Alexander and Ethel Benedict Gutman, Raymond C. Truex, and B. Raj Bhussry; William Hodos dedicates his contribution to the memory of his parents, Morris and Dorothy Hodos, and Walle J. H. Nauta.

In recognition of those special persons in our lives who have been teachers and mentors as well as friends and colleagues, we also dedicate this book to Warren F. Walker, Jr., Theodore J. Voneida, R. Glenn Northcutt, Ford F. Ebner, Sven

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Finally, we dedicate this book to our families, Thomas and Whitney Butler and Nira, Gilya, and Tamar Hodos, who have always given us their loyal support, their patience, and their ceaseless encouragement.

Contents

Preface	xv
Acknowledgments	xix
List of Boxes	xxi

Part One

EVOLUTION AND THE ORGANIZATION OF THE CENTRAL NERVOUS SYSTEM

1 Evolution and Variation	3
----------------------------------	----------

Introduction, 3
Diversity Over Time, 4
Evolutionary Mechanisms, 5
Genetic Factors, 5
Natural Selection, 5
Evolution of the Vertebrate Central Nervous System, 7
Sameness and Its Biological Significance, 8
Analogy, 8
Historical Homology, 8
Homoplasy, 9
Biological Homology, 11
Generative Homology or Syngeny, 12
Analysis of Variation, 13
Cladistic Analysis, 13
Parsimony, 14
Tests of Homology, 15
A Word of Caution, 15
Reconstructing Evolution, 16

2 Neurons and Sensory Receptors	19
--	-----------

Introduction, 19
The Nervous System, 19
Neurons and Sensory Receptors, 20
Transport Within Neurons, 21
Classification of Neurons, 21
Somata, 21

Dendrites, 21
Axons, 23
Synapses, 23
Chemical Synapses, 23
Neuroactive Substances, 24
Electrical Synapses, 26
Volume Transmission, 26
Neuronal Populations, 26
Golgi Type I and II Cells, 26
Nuclei and Planes of Section, 27
Techniques for Tracing Connections Between Nuclei, 27
Receptors and Senses, 28
How Many Senses? 29
Receptors and Awareness, 29
Sensory Experience as a Private Mental Event, 30
Sensory Adaptation, 30
Receptor Types, 30
Mechanoreceptors, 31
Radiant-Energy Receptors, 34
Chemoreceptors, 37
Nervus Terminalis: An Unclassified Receptor, 41
Electroreceptors, 41
Nociceptors, 42
Magnetoreceptors, 43
Topographic Organization, 43
Receptive Fields, 46
The Senses and Evolution of the Central Nervous System, 46

3 The Vertebrate Central Nervous System	49
--	-----------

Introduction, 49
Development of the Brain, 49
Segmental Development of the Vertebrate Brain, 50
Neurogenesis and Migration of Neurons, 54
Cortices and Nuclei, 55
Differing Patterns of Development, 57
Ontogeny and Recapitulation, 60

The Brain and Spinal Cord, 61		Previous Theories of Vertebrate Brain Evolution:	
Cellular Organization of the Central Nervous System, 61		Addition of Structures or Areas, 114	
Regional Organization of the Nervous System, 63		MacLean, 114	
The Spinal Cord, 63		Flechsigs and Campbell, 114	
The Brain, 63		Sanides, 115	
The Meninges and the Ventricular System, 66		Previous Theories of Vertebrate Brain Organization:	
Major Systems of the Brain, 67		New Formation and Reorganization of Circuits, 115	
Sensory Systems, 68		Herrick, 115	
Motor Systems, 68		Bishop, 115	
Nomenclature of the Brain, 69		Ariëns Kappers, 115	
		Bowsher, 115	
		Diamond and Hall, 116	
4 Vertebrate Phylogeny and Diversity in Brain Organization	73	Critique of Previous Theories of Vertebrate Brain Evolution, 116	
Introduction, 73		Parcellation Theory, 117	
Vertebrate Phylogeny, 74		Ebbesson, 117	
Chordate Relationships, 74		Deacon, 117	
Jawless Vertebrates, 74		Current Theories of Forebrain Evolution, 117	
Chondrichthyes, 76		Forebrain Evolution: Experimental Foundations, 117	
Actinopterygii, 76		Karten: Equivalent Cell Hypothesis, 118	
Sarcopterygii, 76		Other Theories of Pallial Evolution, 119	
The Big Picture of Vertebrate Evolution, 84		Perspective, 121	
Two Types of Brain Organization, 84			
Laminar Brains (Group I), 86			
Elaborated Brains (Group II), 87			
Glia and Brain Elaboration, 89			
Laminar and Elaborated Brains across Evolution, 89			
5 Evolution and Adaptation of the Brain, Behavior, and Intelligence	93		
Phylogeny and Adaptation, 93			
Phyletic Studies, 93			
Adaptation Studies, 94			
The Phylogenetic Scale, 95			
The Phylogenetic Tree, 95			
Complexity and Evolution, 96			
Anagenesis, 97			
Grades of Evolutionary Advancement, 99			
Evolutionary Change, 99			
Brain Evolution and Behavioral Adaptation, 100			
Brain Size and Brain Allometry, 100			
Brain Size and Behavioral Adaptation, 105			
Brain Size and Intelligence, 106			
What Is Intelligence? 108			
Summary and Conclusions, 109			
6 Theories of Brain Evolution	113		
Introduction, 113			
Some Common Assumptions, 113			
		Part Two	
		THE SPINAL CORD AND HINDBRAIN	
		7 Overview of Spinal Cord and Hindbrain	127
		Overview of the Spinal Cord, 127	
		Segmentation Within the Spinal Cord, 127	
		Roots and Ganglia, 128	
		Columns of the Spinal Cord, 129	
		Pathways Within the Spinal Cord, 130	
		Reflexes, 131	
		Spinal Autonomy, 133	
		Rhythmic Movements and Central Pattern Generators, 133	
		Overview of the Hindbrain, 133	
		The Obex and the Fourth Ventricle, 135	
		The Pontine Nuclei, 135	
		Ganglia of the Cranial Nerves, 135	
		Organization of the Cranial Nerves, 135	
		Embryology of the Hindbrain and a New Classification of Cranial Nerves, 135	
		Efferent Axons in Afferent Nerves, 136	
		Evolutionary Perspectives on the Spinal Cord and Hindbrain, 136	
		The Transition to Land, 136	
		Tetrapod Locomotor Patterns, 137	

8 The Spinal Cord	139	
The Spinal Cords of Nontetrapods, 139		
Muscles and Locomotion, 139		
Cell and Fiber Columns, 139		
Giant Axons and Escape, 141		
Electromotor Neurons, 144		
The Curious Spinal Cords of Sharks, 144		
Ascending and Descending Pathways, 144		
Reissner's Fiber, 145		
The Organization of the Tetrapod Spinal Cord, 145		
Locomotor Patterns and Spinal Cord Organization, 145		
The Curious Spinal Cords of Birds, 146		
Segmental Organization, 147		
Lamination, 147		
Intrinsic Spinal Neurons, 148		
Somatotopic Organization of the Ventral Horns, 148		
Renshaw Cells, 149		
Axon Columns and Cell Columns, 149		
Marginal Cells, 150		
Accessory Lobes, 150		
Ascending Spinal Pathways, 150		
Descending Spinal Pathways, 150		
Tetrapod Central Pattern Generators, 152		
Evolutionary Perspective, 152		
9 Segmental Organization of the Head, Brain, and Cranial Nerves	157	
"Twelve" Cranial Nerves, 157		
The Vertebrate Head: Segmental Organization, 158		
Head Skeleton, 159		
The Striated Musculature of the Head, 159		
Neural Crest and Placodes, 162		
Segmentation of the Head, 164		
Theoretical Head Segments, 165		
Segmental Organization of the Individual Cranial Nerves, 166		
The Forebrain, 168		
The First Head Segment, 168		
The Second Head Segment, 169		
The Third Head Segment, 169		
The Fourth Head Segment, 169		
The Fifth Head Segment, 170		
10 Functional Organization of the Cranial Nerves	173	
Introduction, 173		
The Cranial Nerves and the Spinal Cord, 173		
The Organization of Sensory and Motor Columns of the Caudal Brainstem, 176		
Afferent Columns of the Brainstem, 177		
Efferent Columns of the Brainstem, 179		
Five Cranial Nerves Rostral to the Brainstem, 180		
General Considerations, 181		
11 Sensory Cranial Nerves of the Brainstem	183	
Introduction, 183		
Dorsal Cranial Nerves: Sensory Components for General Somatosensory Sensation, 183		
Somatosensory Innervation of the Head, 184		
Central Terminations of the Trigeminal Nerve, 185		
The Mesencephalic Division of the Trigeminal System, 185		
Secondary Connections of the Trigeminal Nuclei, 186		
Ventrolateral Placodal Cranial Nerves: Taste, 189		
The Gustatory System, 190		
The Gustatory Nerves and the Nucleus Solitarius, 190		
Secondary Connections of the Gustatory Nucleus and Nucleus Solitarius, 190		
Cyprinid and Silurid Gustatory Specializations, 192		
Dorsolateral Cranial Nerves: Lateral Line and Octaval Systems, 194		
The Lateral Line System, 195		
The Octaval System, 196		
12 Motor Cranial Nerves	205	
Introduction, 205		
Feeding and Swallowing, 207		
The Neural Control of Feeding and Swallowing, 209		
The Communication Systems of Fishes, 211		
The Acoustic Reflex, 213		
Motor Control of Eye Muscles, 214		
The Extraocular Muscles in Jawless Vertebrates, 214		
The Extraocular Muscles in Jawled Vertebrates, 214		
The Intraocular Muscles, 215		
Central Control of the Eye Muscles, 215		
The Oculomotor Complex, 217		
Coordination of Eye Muscle Action, 218		
Evolutionary Perspective on the Hindbrain and Midbrain Cranial Nerves, 218		
13 The Reticular Formation	221	
Introduction, 221		
The Organization of the Reticular Formation, 222		
Neurons of the Reticular Formation, 222		
Giant Reticulospinal Neurons, 223		
Nomenclature of the Reticular Formation, 224		
The Reticular Formation of the Medulla, Pons, and Midbrain, 225		
The Reticular Formation of the Diencephalon, 228		
Pathways of the Reticular Formation, 230		
Chemical Pathways of the Reticular Formation, 232		

The Reticular Formation and Sleep, 234
 Evolutionary Perspective on the Reticular Formation, 236

14 The Cerebellum

241

Introduction, 241
 Overview of the Cerebellum, 241
 Cerebellar Size, 242
 The Various Forms of the Cerebellum, 243
 Corpus Cerebelli, 243
 Electroreception and the Cerebellum, 244
 The Cerebellar Auricle, 245
 Phyletic Development of the Form of the Cerebellum, 245
 The Cerebella of Tetrapods, 246
 The Cerebella of Nontetrapods, 246
 Agnathans and Cartilaginous Fishes, 246
 Ray-Finned Fishes, 246
 The Cerebellar Cortex, 247
 The Purkinje Cell Layer, 247
 The Granule Cell Layer, 249
 The Molecular Layer, 253
 Afferent Inputs to the Cerebellar Cortex, 253
 Interconnections Within the Cerebellar Cortex, 255
 The Precerebellar Nuclei, 256
 Cerebelloid Structures Associated With the Cerebellum in Nontetrapods, 257
 The Exceptional Cerebella of Weakly Electric Fishes, 259
 Cerebellar Efferents and the Deep Cerebellar Nuclei, 260
 Evolutionary Perspective, 262
 Functions of the Cerebellum, 262

Part Three

THE MIDBRAIN

15 Overview of the Midbrain

267

Introduction, 267
 The Isthmus, 268
 The Tegmentum, 273
 The Tectum, 273

16 Isthmus

275

Introduction, 275
 Nuclei of the Raphe, 275
 Group I, 275
 Group II, 275
 Evolutionary Perspective, 277

Locus Coeruleus, 277
 Group I, 277
 Group II, 277
 Evolutionary Perspective, 278

Nucleus Isthmi, 281

Group I, 281
 Group II, 281
 Evolutionary Perspective, 283

Isthmo-Optic Nucleus, 283

Group I, 283
 Group II, 283
 Evolutionary Perspective, 284

Midbrain Locomotor Region and Pedunculopontine Tegmental Nucleus, 284

Group I, 284
 Group II, 284
 Evolutionary Perspective, 285

Interpeduncular Nucleus, 285

Group I, 285
 Group II, 285
 Evolutionary Perspective, 285

17 Tegmentum and Tori

289

Introduction, 289
 Mesencephalic Nucleus of the Trigeminal Nerve, 289
 Group I, 289
 Group II, 290
 Evolutionary Perspective, 290
 Red Nucleus and Related Nuclei, 290
 Group I, 290
 Group II, 290
 Evolutionary Perspective, 292
 Substantia Nigra and Ventral Tegmental Area, 292
 Group I, 293
 Group II, 294
 Evolutionary Perspective, 303

Torus Lateralis, 304

Group I, 304
 Group II, 304
 Evolutionary Perspective, 304

Torus Semicircularis, 304

Group I, 304
 Group II, 305
 Evolutionary Perspective, 306

18 Optic Tectum

311

Introduction, 311
 Overview of Tectal Organization, 311
 Overview of Tectal Connections, 312
 The Optic Tectum in Group I Vertebrates, 315

Lampreys, 315
Squalomorph Sharks and Ratfishes, 316
Nonteleost Ray-Finned Fishes, 316
Amphibians, 319
The Optic Tectum in Group II Vertebrates, 321
Hagfishes, 321
Galeomorph Sharks, Skates, and Rays, 322
Teleosts, 322
Amniotes, 325
Evolutionary Perspective, 334

Part Four

THE FOREBRAIN: DIENCEPHALON

19 Overview of the Forebrain	343
Introduction, 343	
Nomenclature of the Forebrain in Amniotes, 344	
The Diencephalon, 344	
Pretectum, 344	
Posterior Tuberculum, 344	
Epithalamus, 345	
Dorsal Thalamus, 346	
Ventral Thalamus, 347	
Hypothalamus and Preoptic Area, 352	
The Telencephalon: Pallium, 352	
The Telencephalic Pallium of Mammals, 353	
The Telencephalic Pallium of Nonmammalian Amniotes, 361	
The Telencephalon: Subpallium, 364	
The Ventrolateral Telencephalon of Anamniotes, 364	
The Ventrolateral Telencephalon of Mammals, 364	
The Ventrolateral Telencephalon of Nonmammalian Vertebrates, 368	
The Septum, 369	
20 Pretectum, Accessory Optic System, and Migrated Posterior Tuberculum	373
Introduction, 373	
Pretectum, 373	
Group I, 374	
Group II, 375	
Accessory Optic System, 389	
Group I, 391	
Group II, 392	
Evolutionary Perspective, 394	
Migrated Posterior Tuberculum, 396	
Group I, 396	
Group II, 396	
Evolutionary Perspective, 399	

21 Epithalamus	407
Introduction, 407	
Epiphysis, 407	
Habenula, 409	
Evolutionary Perspective, 414	
22 Dorsal Thalamus	417
Introduction, 417	
Collothalamic Auditory System, 418	
Group I, 418	
Group IIA, 418	
Group IIB, 420	
Collothalamic Visual and Somatosensory Systems, 426	
Group I, 427	
Group IIA, 430	
Group IIB, 430	
Lemnothalamus, 432	
Group I, 432	
Group IIA, 434	
Group IIB, 434	
Evolutionary Perspective, 437	
Collothalamus, 437	
Lemnothalamus, 437	
A New Definition of the Dorsal Thalamus in Vertebrates, 439	
23 The Visceral Brain: The Hypothalamus and the Autonomic Nervous System	445
Introduction, 445	
The Hypothalamus, 445	
The Hypothalamus and the Endocrine System, 446	
Circumventricular Organs, 449	
Biological Rhythms, the Epiphysis, and the Hypothalamus, 449	
The Hypothalamus and the Limbic System, 450	
The Preoptic Area, 450	
The Hypothalamus in Anamniotes, 451	
Jawless Fishes, 451	
Cartilaginous Fishes, 451	
Actinopterygians, 451	
Sarcopterygians, 455	
The Hypothalamus in Amniotes, 455	
Connections of the Hypothalamus in Reptiles and Birds, 456	
Connections of the Hypothalamus in Mammals, 457	
Functions of the Hypothalamus, 460	
The Autonomic Nervous System, 460	
Autonomic Neurochemistry, 462	
Amniotes, 462	
Anamniotes, 462	
Evolutionary Perspective, 462	

Part Five**THE FOREBRAIN: TELENCEPHALON****24 Basal Telencephalon 471**

Introduction, 471
 The Striatopallidal Complexes, 472
 Group I, 472
 Group IIA, 476
 Group IIB, 477
 The Striatum Amygdala, 487
 Cholinergic Neuronal Populations of the Basal Telencephalon, 488
 Evolutionary Perspective, 489

25 Nonlimbic Pallium 495

Introduction, 495
 The Nonlimbic Pallium in Group I Vertebrates, 496
 The Nonlimbic Pallium in Group IIA Vertebrates, 498
 Neuroanatomical Organization, 498
 Behavioral Issues, 501
 The Nonlimbic Pallium in Amniotes, 501
 Mammals: Neocortex, 501
 Mammals: Claustrum-Endopiriform Formation and Frontotemporal Amygdala, 504
 Reptiles and Birds, 504
 Ascending Sensory Pathways to the Pallium in Amniotes, 507
 Pallial Evolution and Persistent Questions of Homologies, 510

26 Visual Forebrain in Amniotes 523

Introduction, 523
 Ipsilateral Retinal Pathways and Stereoscopic Vision, 524
 Visual Pathways to the Telencephalon in Mammals, 524
 Lemnothalamic Visual Forebrain, 524
 Collothalamic Visual Forebrain, 536
 Pathways to the Visual Telencephalon in Reptiles and Birds, 537
 Lemnothalamic Visual Pathways, 538
 Collothalamic Visual Pathways, 540
 Evolutionary Trends in the Visual System of Amniotes, 540

27 Somatosensory and Motor Forebrain in Amniotes 547

Introduction, 547
 The Somatosensory and Motor Forebrain of Mammals, 547
 The Ventral Tier Nuclei of the Dorsal Thalamus, 548

Somatosensory Lemnothalamus, 548
 Somatosensory Collothalamus, 548
 Motor Lemnothalamus, 548
 Afferents to Somatosensory Cortex, 549
 Efferents of Somatosensory Cortex, 549
 Pain Pathways, 549
 Somatotopic Organization, 552
 Motor Cortex, 557
 Multiple Motor Representations of the Body, 558
 The Cortical Eye Fields, 558
 Afferents and Efferents of the Motor Cortex, 558
 The Somatosensory and Motor Forebrain of Nonmammalian Amniotes, 559
 Somatosensory System, 559
 Motor System, 564
 Evolutionary Perspective, 566

28 Auditory and Vocal Forebrain in Amniotes 571

Introduction, 571
 Location of Sound Sources, 571
 Echolocation, 572
 Auditory Channels for Time and Intensity, 573
 Design Features of the Auditory System, 574
 Topographic Organization, 574
 Bilateral Interaction in the Auditory Pathway, 574
 Descending Auditory Pathways, 574
 Auditory Pathways in Tetrapods, 574
 Auditory Telencephalon, 577
 Columnar Organization, 577
 Mammals, 577
 Reptiles and Birds, 579
 Vocal Telencephalon, 580
 Vocalization and Hearing, 581
 Anurans, 582
 Reptiles and Birds, 583
 Mammals, 587
 Evolutionary Perspective, 589

29 Terminal Nerve and Olfactory Forebrain 593

Introduction, 593
 Olfactory System, 593
 Group I, 594
 Group II, 595
 Vomeronasal System, 601
 Terminal Nerve, 605
 Evolutionary Perspective, 606

30 Limbic Telencephalon 611

Introduction, 611
 The Limbic Pallium in Amniotes, 612

Group I, 612	
Group IIA, 613	
The Limbic Pallium in Amniotes (Group IIB), 617	
Limbic Pallium of Mammals, 619	
Limbic Pallium in Nonmammalian Amniotes, 623	
Limbic Subpallium: Septum, 628	
Evolutionary Perspective, 629	

Part Six

CONCLUSION

31 Evolution of Brains: A Bilaterian View	637
Introduction, 637	
Invertebrate Brains and the Inversion Hypothesis, 638	
Insect Brain Organization, 639	
Urbilateria and the Ancestral Condition of Bilaterian Brains, 641	
Deuterostomes and Dorsoventral Inversion, 641	

Brain Evolution within Chordates, 644	
The Origin of Vertebrates, 649	
Haikouella, 650	
Sensory System Evolution in the Vertebrate Lineage, 652	
Organization of the Vertebrate Brain, 653	
The Advent of Jaws, 655	
Onto the Land and Into the Air, 656	
Theories of Vertebrate Brain Evolution, 657	
How Vertebrate Brains Evolve, 657	

Appendix: Terms Used in Neuroanatomy	665
Introduction, 665	
Direction and Location Terms, 665	
Planes of Section, 666	
Neuroanatomical Names, 668	
Derivation of Terms, 668	
Glossary	671
Index	679

Preface

What Is This Book About?

This book is about the central nervous system of those animals that possess backbones—the vertebrates—and how evolution has shaped and molded their bodies and their nervous systems, allowing them to thrive in their particular environments or to take advantage of new environmental opportunities. Thus, it is a book about the relationship between structure and function and about survival through effective design. It is a book about the past as well as the present and about the history of vertebrate nervous system evolution, to the extent that we can read that history from the present state of these animals.

Who Is This Book For?

This book has been written first and foremost for neuroscience students at the graduate or advanced undergraduate level. We have presumed that the reader will have taken one or more introductory undergraduate biology courses or otherwise be familiar with this material. In a more general sense, this book is also for anyone who is interested in the anatomy of the nervous system and how it is related to the way that an animal functions in its world, both internal and external.

This book is intended as an introductory work rather than as a handbook or reference work that scientists might refer to in their professional writing. We have modeled this book on several textbooks designed for advanced undergraduate to graduate levels: *Functional Anatomy of the Vertebrates: An Evolutionary Perspective* (Second Edition) by W. F. Walker, Jr. and K. F. Liem (Saunders College Publishing, Fort Worth, TX, 1994); *Hyman's Comparative Vertebrate Anatomy* edited by M. H. Wake (The University of Chicago Press, 1979); *The Human Brain and Spinal Cord* by L. Heimer (Springer-Verlag, New York, 1983); *Core Text of Neuroanatomy* by M. B. Carpenter (Williams and Wilkins, Baltimore, 1991); *An Introduction to Molecular Neurobiology* by Z. W. Hall (Sinauer Associates, Sunderland, MA, 1992); and *Principles of Neuroscience* (Third Edition) by E. R. Kandel, J. H. Schwartz, and T. M. Jessell (Appleton and Lange, Norwalk, CT, 1991). In keeping with the format of these texts, we have not cited references in the body of the text, but at the end of each chapter we have listed the references from which we drew material and additional papers that may interest the reader. Our aim has been to introduce the reader to the field and to synthesize information into a coherent overview, rather than to present an extensive catalog of individual data.

In keeping with the introductory nature of this work, we largely have omitted details on whether and/or where particular projections cross the midline of the nervous system. In some cases, where this information is of particular importance, we have included it. However, in most cases, we leave it to the interested reader to glean such details from other sources.

This is a book that we hope will be of interest to the general scientific reader and the nature enthusiast, as well as to advanced undergraduate or beginning graduate students in the neurosciences. Physicians and others with knowledge of the human central nervous system should also find much of interest here. To our colleagues who are specialists in the field of comparative neuroanatomy, we say that this is not the book that you might write; this is the book that students should read to give them the background to read your book and other scholarly publications in neuroanatomy and brain evolution.

Apropos of this aim and since the time of the first edition of this textbook, a truly remarkable contribution to the literature of comparative neuroanatomy was made by Rudolf Nieuwenhuys, Hans ten Donkelaar, and Charles Nicholson with the publication of their comprehensive and encyclopedic set of three volumes on *The Central Nervous System of Vertebrates* (1998, Springer-Verlag, Berlin). These volumes cover the subject and the literature in far greater depth and breadth than could or should be included in a textbook. We have benefited greatly from the material in these volumes in writing the second edition of this book. In updating material, there is the constant temptation to add more and more detail, and in the process, forsake the original purpose. We thus have endeavored to tread a fine line between updating and maintaining the introductory level. We hope that this book will continue to fill its intended role as an introductory work, allowing the reader to then delve into the Nieuwenhuys et al. volumes as well as the primary literature for much more extensive and detailed treatments of a multitude of topics.

What Can Be Learned About the Human Brain From a Book About the Brains of Many Different Vertebrates?

During the past four decades, a great explosion of information about the anatomy of the brains of nonhuman and especially nonmammalian vertebrates has taken place. One of the lessons to emerge from this wealth of new data has been the reversal of the nineteenth century view that a dramatic change in brain evolution occurred with the evolution of mammals in

general and humans in particular. In other words, once the powerful tools of modern neuroanatomy were applied to the brains of birds, fishes, reptiles, and amphibians, many of the same patterns of cell groups and their interconnections that were known to be present in mammals (including primates) were found to be present in nonmammalian vertebrates as well. Thus, comparative neuroanatomists came to recognize that the evolution of the vertebrate central nervous system had been far more conservative than earlier investigators had realized.

To be sure, great differences in specialization of the brain exist between animals that have become adapted to very different modes of existence. Indeed, those differences in form and function are what make the study of comparative neuroanatomy and brain evolution so fascinating—a fascination that we hope to share with you. In spite of these differences, however, all vertebrate central nervous systems share a common organizational scheme so that someone who is familiar with the brain of any vertebrate will also be on familiar ground when first encountering the brain of any other species. Someone who has read this book and retained the general principles of brain anatomy and organization that it presents will have little difficulty reading a medical school textbook of human neuroanatomy because much of it will be familiar both in overall conception and in many of the details.

What Is New in This Book and How Does It Differ from Other Texts?

The first edition of this book incorporated several new approaches to the subject matter of comparative neuroanatomy and the orientation with which we study it. These new approaches, which have been maintained and/or further developed in this second edition, include

- A recent reevaluation of the cranial nerves of vertebrates and their derivation and organization
- A new organizational approach to the various groups of vertebrates based on the degree of elaboration in their central nervous systems rather than the traditional, *scala naturae*-like ranking
- New insights into the organization and evolution of the dorsal thalamus and dorsal pallium in the forebrain
- A new and comprehensive overview of brain evolution in vertebrates that encompasses many of the evolutionary and developmental topics covered in the rest of the text

The first of these new approaches is based on the work of Northcutt, Baker, Noden, and others, on the organization of the cranial nerves. While constituting a radical departure from the established, traditional list of twelve cranial nerves with their functional components, we feel that this new approach is a marked improvement for two reasons: First, it takes into account additional cranial nerves, both long known and newly recognized ones, that are found in many vertebrates but are not included in the “traditional twelve.” Second, it is based on embryological development, including gene expression patterns, and thus provides a coherent accounting of the segmentation of the head itself and of its component parts, including both the brain and other tissues (particularly the

neural crest, epithelial placodes, and paraxial mesoderm). Chapter 9 on the embryology of the cranial nerves in relation to head segmentation covers this newly developed approach to cranial nerve organization and is crucial to understanding the subsequent chapters on the cranial nerves themselves.

The second departure from tradition that we took in the first edition and have retained here is the order in which various groups of vertebrates are considered in the chapters on the various regions of the nervous system. This approach is based on the range of variation in brain structure within each of the major groups of vertebrates. It is intended to overcome the erroneous but culturally ingrained idea of a single, simple-to-complex, linear series of evolutionary stages leading from fish to frog to rat to cat to monkey to human, i.e., the myth of a *scala naturae*. Chapter 4 specifically addresses this issue.

A great diversity in brain organization has been achieved independently at least four separate times within four separate radiations of vertebrates; our approach is designed to highlight both the diversity itself and its multiple, independent development. Thus, in a number of the chapters on brain regions and systems, particularly in the midbrain and forebrain, we first consider and compare those species within each radiation in which the brain has relatively simple cellular organization, as for example, lampreys, dogfish sharks, gars, and frogs. We then consider and compare those species within each radiation in which the brain has relatively complex cellular organization, as for example, hagfishes, skates, teleost fishes, and amniotes (mammals, reptiles, and birds). We hope to convince the reader that the development of a more complex brain has been accomplished not just once for the “ascent of man,” but multiple times. Moreover, we will show that mammals (including primates) do not always have the most sophisticated brain systems.

In line with this point, other chapters, including “Evolution and Variation,” “Evolution and Adaptation of the Brain, Behavior, and Intelligence,” and “Theories of Brain Evolution,” seek to dispel further the myth of *scala naturae* and to deal with the actual range of variation in line with the known facts and processes involved. In this context, we hope that the reader will come to understand that, whereas some vertebrates have simpler brains than others, all living vertebrates are equally successful in that they are alive and adapted to their environments.

A third new approach taken for the first edition and maintained here concerns the evolution of two major parts of the forebrain, the dorsal thalamus and the dorsal pallium, particularly in amniote vertebrates. Two fundamentally different divisions of the dorsal thalamus recently have been recognized in all jawed vertebrates: one that predominantly receives direct, lemniscal sensory and related inputs, called the lemnothalamus, and one that predominantly receives sensory inputs relayed to it via the roof of the midbrain, called the collothalamus. These lemnothalamic and collothalamic divisions of the dorsal thalamus have recently gained validation from differential patterns of gene expression during development. Correspondingly, two major divisions of the pallium in amniote vertebrates that receive their respective inputs predominantly from the lemnothalamic and collothalamic divisions of the dorsal thalamus have been recognized as well. The way in which a number of the chapters on the forebrain have been

organized and the material presented in them are based to some extent on these new concepts of forebrain evolution. Finally, new insights into the evolution of the brain, not just in vertebrates but among some of the invertebrate chordates as well, are presented in the last chapter of this book. Recent findings on genetic patterning of central nervous system structure and on the anatomy of the brain and head region in the cephalochordate *Branchiostoma*, as well as anatomical evidence from the recently found fossils of the chordate *Haikouella*, allow for some of the features of the brain in the earliest vertebrates to be identified. A new survey of brain evolution is presented. For context, brain organization in some invertebrates is surveyed, particularly in terms of gene expression patterns, which are strikingly similar to those in vertebrates. Then vertebrate brain evolution is discussed, beginning with a few but significant features that can be identified in the common ancestors of cephalochordates and vertebrates, identifying

additional features that were present in the earliest vertebrates, including two novel tissues of the head (neural crest and placodes) and a number of cranial nerves associated with them, and then tracing the separate evolutionary histories of the brain in the major radiations of extant vertebrates.

For the second edition, a recently proposed model of the transition to vertebrates that specifies the gain of paired eyes and elaboration of the diencephalon and hindbrain before most of the elaboration of neural crest and placodal tissues occurred to produce the peripheral nervous system has been included. This model was recently given strong support by newly discovered fossil evidence from the chordate *Haikouella*. Also, the striking similarities of patterning gene expression across all bilaterally symmetrical animals studied, from mice to fruit flies, and their implications for the evolution of rostrocaudally and dorsoventrally organized central nervous systems are discussed.

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List of Boxes

Box 1-1.	Morphogenetic Fields and the New “Evo-Devo” Synthesis	7	Box 14-2.	Is There More Than One Cerebellum in the Brain?	258
Box 1-2.	Field Homology	10	Box 14-3.	Myelinated Dendrites in the Electrosensory Lateral Line Lobe of Mormyrids	260
Box 2-1.	Dome Pressure Receptors	33	Box 18-1.	Magnetoreception and the Optic Tectum	313
Box 2-2.	Another Taste System?	38	Box 18-2.	Tectal Ganglion Cells With Bottlebrush Dendritic Endings: Questions About Tectal Lamination	332
Box 2-3.	Isomorphic Topographic Maps	44	Box 21-1.	A Strange Nucleus in Some Ray-Finned Fishes	413
Box 3-1.	What Is “Neo” About Neocortex, and What Is “Iso” About Isocortex?	58	Box 22-1.	Evolutionary Origin of the Lemnothalamic Visual Pathway: New Perspectives	433
Box 4-1.	Hagfishes: Invertebrate Chordate or Legitimate Vertebrate?	75	Box 23-1.	Hypothalamic Peptides and Proteins	448
Box 4-2.	The Early Divergence of Synapsids	81	Box 25-1.	Evolution of Sensory Cortices Across Mammals	505
Box 4-3.	Turtles: Welcome Home to Diapsid-ville!	82	Box 25-2.	Complex Cognitive Functions of Parietal and Prefrontal Cortical Areas in Humans	506
Box 5-1.	Did the Dinosaurs Have Small Brains?	103	Box 25-3.	The Impressive Cognitive Abilities of Birds	514
Box 5-2.	A New Taxonomic Method Based on Brain Allometry	104	Box 26-1.	Evolution of the Skull and Evolution of Frontal Vision	524
Box 5-3.	Are There Constraints on Brain Growth?	106	Box 26-2.	Functional Streams in the Avian Tectofugal Pathway	542
Box 5-4.	Brain Evolution and Consciousness	107	Box 27-1.	What Is “Neo” About the Neospinothalamic Tract?	553
Box 8-1.	Neuroactive Substances in the Spinal Cord	142	Box 28-1.	Sexual Dimorphism in the Auditory and Vocal Control Systems	586
Box 8-2.	A Neuroendocrine Organ in the Spinal Cord: The Caudal Neurosecretory System	145	Box 29-1.	The Olfactory and Vomeronasal Systems of Snakes	604
Box 8-3.	Sexual Dimorphism in the Spinal Cord	151	Box 30-1.	The Hippocampus and the Amygdala of Goldfish	616
Box 11-1.	The Marvelously Versatile Trigeminal Nerve	187	Box 30-2.	Imaginative Images of the Hippocampus	618
Box 12-1.	The Unusual Abducens Nucleus of Goldfish: A General Somatic Efferent Nucleus “Gone Walkabout”	216	Box 31-1.	Eyes, Eye Evolution, and <i>Pax-6</i>	642
Box 12-2.	The Ciliary Muscles of Diving Birds: A Magnificent Adaption	217			
Box 13-1.	Neuroactive Substances and Sleep	235			
Box 13-2.	Constant Vigilance and Unihemispheric Sleep	237			
Box 14-1.	Lugaro Cells and Unipolar Brush Cells	254			

Part One

EVOLUTION AND THE ORGANIZATION OF THE CENTRAL NERVOUS SYSTEM

Evolution and Variation

INTRODUCTION

One of the primary fascinations of the natural world is the vast diversity of living organisms within it. Diversity of organisms and their many body parts is a hallmark of biology. Biological diversity has been produced by the process of **natural selection**, part of which is a reflection of changing climates, geophysical phenomena, and habitats. The pressures of natural selection act on spontaneous variations of the phenotypes that occur within a population and are the result of mutational changes within the genes.

For the study of biological diversity, we need to recognize the natural groupings to which individual organisms belong. A **species** is usually defined as a naturally interbreeding set of individual organisms or set of populations of organisms. The English words “species” and “special” derive from the same Latin term *specialis*, and in fact each species is distinguished by its particular, special feature(s) that is/are unique to it. The next level of phylogenetic classification is that of **genus**, which is a set of species that are more closely related to each other than to species outside the genus. Additional examples of levels are those of **family**, **order**, **class**, and **phylum**. Also, various intermediate levels, such as subfamily, infraorder, supraorder, and so on, are employed as appropriate. Even within a species, various subspecies can be recognized. The term **taxon** applies to any defined, natural group of organisms, such as a species, order, or class. The term **clade** can also be used to refer to such defined natural groups. The terms taxon and clade are usually and best used to apply to **monophyletic groups**, which are groups that include all of the descendants of a specified common ancestor and no other members. In

practice, often only the **extant** (living) descendants are addressed.

Our current understanding of biological diversity began with the theory put forth by Charles Darwin (and independently by Alfred Russel Wallace) in 1858–1859. This theory states that a process of evolution by natural selection has produced the variation that is documented by the fossil record and among extant species. The source of the variation upon which natural selection acts was not identified until the science of genetics was established by the pioneering work of Gregor Mendel, who in 1865 formulated the principle of particulate inheritance by the means of transmitted units or genes, and the later work of Theodosius Dobzhansky and others in the first half of the twentieth century.

Modern evolutionary theory embodies the work of Darwin in the context of genetics, molecular biology, and other relevant sciences. This interrelationship of disciplines was termed an **evolutionary synthesis** by Julian Huxley in 1942; it refers to the recognition that both gradual evolutionary changes and larger evolutionary processes, such as speciation, are explainable in terms of genetic mechanisms. Since that time, a substantial body of work in genetics, systematic biology, developmental biology, paleontology, and related fields has yielded new and more complex insights on this subject. The title of a recent book by Niles Eldredge (1985), *Unfinished Synthesis*, reflects the continuing debate within the field.

Until Darwin’s publication of his views, most Western scientists believed that most or all species of wild animals living at that time had been unchanged since their creation by a deity. Darwin’s idea that living creatures had evolved over long periods of time was accepted fairly readily. Some resisted the

idea of humans being animals in continuity with nature, that is, that humans are related to any other animals, such as apes and monkeys. That evolution is a directionless process employing natural selection is a concept that has been accepted by some but resisted with vigor by others, even today.

The idea that evolution is progressive in the sense that progress or continuous improvement occurs over time is seductive and comforting. It is seductive in its appeal to the egocentricity of our species and comforting as a source of moral principles. The Aristotelian concept of a *scala naturae* that living animals can be arranged in a continuous, hierarchical, ladder-like progression with humans at the pinnacle embodies this appeal, as does the Judeo-Christian tradition of creation that culminates with the human species. Julian Huxley promoted the idea that, although evolution was without purpose, it was progressive. He believed that ethical principles and the meaning of human existence could be derived from the position of humans at its pinnacle.

The *scala naturae* concept of progressively ascending scales of life forms, such as the fish-frog-reptile-rat-cat-monkey-human sequence, is seen as intuitively correct. The pervasive flaw in all such rankings is that they are made from an anthropocentric point of view. The anthropocentric scale, however, is of no greater scientific value in an evolutionary context than one based, for example, on our assessment of the animals' beauty. The appeal of the idea of progress over evolution is based on the fact that progress itself, like beauty, is a human concept and value; it is not, however, a biological principle.

Inherent in the notion of a scale of nature is the idea that each animal has a natural rank on this scale. The more "advanced" animals (humans and the ones seemingly closest to humans) occupy ranks high on the scale, and those that seem to bear less resemblance to humans are relegated to the lower ranks. Thus, we have come to refer to some animals as "the higher vertebrates" and others as "the lower vertebrates," or "the submammalian vertebrates." Unfortunately, terms like "higher," "lower," and "submammalian" represent only homocentric value judgments; they are thus inappropriate ways of comparing animals and have no place in the vocabulary of evolutionary biology. Many extant species of vertebrates are only distantly related to humans and resemble them very little; nevertheless, these animals are just as successful and well adapted to their environments as humans and their closest relatives are to their own environments. The simple fact that animals are different does not confer any rank to them relative to each other.

Many humans consider the human species as "special," different in some way and standing apart from all other species. As noted above, the word "special" and "species" are derived from the same Latin term, so in that sense, *all species are special*. Thus, to the extent that we are a species, we are special by definition. The perspective of William S. Gilbert and Sir Arthur Sullivan, in their operetta *The Pirates of Penzance*, is relevant here: "If everybody's somebody, then no one's anybody." *Scala naturae* thinking that views any one species as superior to all others is in fact one of the greatest impediments to understanding the biological world and to appreciating the place of our own species within it. Evolution does not create superior and inferior taxa; it simply creates diversity.

DIVERSITY OVER TIME

Biological diversity is a result of natural selection acting on random variations within populations of organisms. The degree of biological diversity has increased over time in some ways. For example, twice as many species of marine animals (invertebrate and vertebrate) exist today as existed in the Paleozoic era. In other ways, however, biological diversity has dramatically decreased over time. In the Paleozoic era, the number of groups of higher taxonomic rank (more inclusive categories) was far greater than the number that exists today. Diversity in the range of basic body plans has decreased, whereas the diversity of species having any of the few, extant, basic body plans has increased. The greater number of extant species is grouped within the fewer number of higher categories.

One explanation for this more complex pattern of evolutionary change focuses on processes that tend to eliminate extremes in variation, such as competition under conditions of natural selection. Animals with the more successful body plans would ultimately survive, and the number of higher categories thus decreases over time. A second explanation involves the random process of **extinction**. To consider this possibility, we need to examine evolutionary history in terms of the extreme physical forces that shape it.

Extinctions of varying degree repeatedly occur and profoundly affect biological evolution. Some extinctions are of modest degree and limited extent, happening to isolated populations due to normal environmental fluctuations or accidental factors. Species most resistant to environmental fluctuations tend to be those with individuals that have larger bodies, longer lives, and a greater degree of social interaction related to breeding behaviors. Other extinctions are of greater consequence and related to **habitat fragmentation** caused by such factors as tectonic shifts, temperature changes, alteration in rainfall patterns, and changes in oceanic level. When habitat fragmentation occurs, species more resistant to extinction are those that are herbivorous versus carnivorous and, among carnivores, of smaller body size. Those species with more strictly defined habitat requirements—**habitat specialists**—are more prone to extinction than species that are **habitat generalists**. Species with populations of smaller size or lesser density are likewise more prone to extinction than those of greater size and/or density.

Of the greatest consequence are mass extinctions of hundreds or thousands of species, such as those that occurred at the end of the Permian and the Cretaceous periods. Not only are mass extinctions dramatic and of momentous impact on biological flora and fauna, but they appear to occur with a regular periodicity. Mass extinctions have recurred on a cycle of about 26 million years for at least the last 225 million years. The Cretaceous extinction occurred 65 million years ago. To account for a cycle on such a long time scale, extraterrestrial causes, such as asteroid or comet impacts, have been considered, and evidence from the distribution of iridium, a relatively rare element of extraterrestrial (meteoritic) origin, in the earth's surface supports this possibility. A recurring disturbance of the Oort cloud—the cloud of comets that circle the sun—could release comets that could then impact the earth with catastrophic results.

In mass extinctions, some species and groups of species have better chances of survival than others. Categories of taxa that have a greater number of species (**species-rich clades**) tend to be composed of habitat specialist species, species that have become specialized for survival in a particular habitat, which are thus more susceptible to extinction if the habitat changes suddenly. In contrast, the habitat generalist species tend to be in taxonomic categories with a fewer number of species (**species-poor clades**), have wider geographic ranges, and can more readily shift habitats if conditions change.

In normal times, species-rich clades undergo a net increase in species number, offsetting losses due to limited environmental fluctuations, accidents, and habitat fragmentation. This speciation has a pattern of punctuated equilibrium—rapid change followed by a longer period of little or no change, as discussed below. Species-poor clades, on the other hand, have a lower rate of speciation but are more resistant to environmental and habitat assaults. This balance permits both types of clades to flourish in the intervals between mass extinctions. In mass extinctions, the species-rich clades are more vulnerable, and thus over time, fewer higher categories survive. More species arise in at least some of the remaining higher categories due to new waves of speciation following each period of mass extinction. Biological evolution is thus the net result of multiple independent processes.

EVOLUTIONARY MECHANISMS

Evolution can be defined simply as a *change over time*. In biological systems, random genetic variation occurring within a population allows for phenotype variation, which natural selection can then act upon. Darwin recognized that evolution occurs as a consequence of two separate processes. The first process, which we know today to encompass mutations and genetic recombinations as well as other factors, is a random process that produces variability. The second process, natural selection, is not random but rather opportunistic, and it acts on this variability. Natural selection acts on populations, affecting the frequency of particular genes within the population, rather than on individuals.

Genetic Factors

Mutations and changes in the frequency of certain gene alleles, that is, alternate forms of the gene (dominant vs. recessive), account for diversity within an interbreeding population. The individual members of the population are similar but not identical. Because a gene may exist in a large variety of allelic forms but an individual animal has only one pair of alleles for each gene, any given individual possesses only a small fraction of the total genetic variation that is stored in the population as a whole.

The relative frequencies of alternative alleles and genotypes reach equilibrium and then tend to remain constant in a large, randomly mating population. Despite this tendency, changes in the frequencies of different alleles do occur over succeeding generations. In addition to mutations, factors that affect the frequency of alleles in a species include **genetic recombination**, **gene flow**, and **isolating mechanisms**.

Gene recombination assembles an existing array of allelic forms of different genes into a variety of combinations. This does not increase the frequencies of these alleles but does increase variability. While mutation is the ultimate source of genetic variation, recombination generates numerous genotypic differences among individuals in a population. Consequently, recombination provides a large number of the variations acted upon by natural selection.

Gene flow is a change in the frequency of particular alleles caused by individuals of the same species migrating into and interbreeding within a given population. Gene flow is essential to maintaining various populations as members of a single species, since the most important aspect of the definition of a species is that it consists of a set of populations that actually or potentially interbreed in nature. Gene flow is responsible for genetic cohesion among the various populations that form the species. This process is a stabilizing influence on genetic variation and is responsible for the relatively slow rate of evolution that occurs in common, widespread species.

Biological mechanisms that isolate one population from another reproductively are in direct contrast to gene flow and define the limit of the species. Geographic isolation, such as islands separated from each other by the ocean or a peninsula being isolated as an island due to a rise in the level of the ocean, can result in changes in gene frequencies between the two populations. A small number of individuals that becomes isolated from the rest of the population will not necessarily have the same alleles in the same frequency distribution as the whole original population, resulting in a shift in allelic frequencies in the isolated population. Examples of such isolated populations are various species of birds on various islands in the Galapagos, Hawaiian, and other similar island groups. If the geographic isolation eventually ceases, reproductive isolation may nevertheless be maintained by newly established mechanical incompatibilities of the male and female or by behavioral isolation caused by differences in mating ritual or species recognition cues that exclude some formerly potential mates.

Natural Selection

Natural selection acts on the variability and establishes certain variant types in new frequencies within a given population. Natural selection is the increase in frequency of particular alleles as a result of those alleles enhancing the population's ability to survive and produce offspring. The **fitness** of a variant is a measure of how strongly the variant will be selected for, that is, how adaptive it is. Thus, a novel variant that enables a population to capitalize on a vacant niche may rapidly establish itself. Alternatively, selective pressures that are too strong, such as a relatively sudden decrease in ambient temperatures during an ice age, may result in extinction of populations. In such a case, the variability within the population is simply not extensive enough to fortuitously have the number of variants that would allow for selection of adaptations to the cold.

If a mutant allele appears infrequently in a large population, the initial frequency of the allele will be low and will tend to remain low. If a mutant allele appears in a single individual and has no selective advantage or disadvantage, it can by chance alone readily become extinct. On the other hand, if it

even slightly enhances the ability of its bearer to live and reproduce, it will increase in frequency. Selection is the most important means by which allele frequencies are changed. Natural selection can be considered to consist of the differential, nonrandom reproduction of particular alleles. As alleles are parts of whole genotypes, selection can also be thought of as the differential and nonrandom reproduction of particular genotypes.

Darwin considered natural selection to mean differential mortality. Contemporary evolutionists look upon it as differential reproduction. Although natural selection does frequently take the form of differential mortality, other strategies occur as well, such as increasing the number of offspring produced or improving the chance of successful mating by increasing efficiency in getting food or evading predators. Differential mortality can be regarded as one form of differential reproduction, if, for example, some animals do not survive long enough to reproduce.

Gene alleles most often have multiple effects, that is, they are **pleiotropic**. Some of the characteristics determined by an allele may be advantageous to the individual, while others may be disadvantageous. An individual carrying an allele (A) might have a selective advantage over another individual carrying its matching allele (A'), but might be inferior to the phenotype of the second individual in some other character produced by allele A. If individuals carrying the allele A have a net superiority over individuals carrying the allele A', then allele A will increase in frequency despite its deleterious side effects.

The discussion thus far has been primarily concerned with selection of single alleles, but the same principles can be extended to encompass combinations of two or more genes. Many adaptations are based not on single genes but on multiple genes or gene combinations and the resultant phenotype on which selection acts. Populations of organisms exist in a particular environment to which they must be fitted or adapted in order to live and reproduce successfully. If the environment remains stable and the population is highly adapted, selection operates primarily to eliminate peripheral variants and off-types that arise by mutation or recombination. If a change occurs in the environment, one or more of the peripheral variants may be better adapted to the new conditions than those with the more normal genotype. Selection now takes a different form, favoring the formerly peripheral variants and eliminating some of the standard genotypes.

Since natural selection acts on a population rather than any individual, traits such as "altruism" can be selected for. For example, in many species, an individual animal may do work or even sacrifice itself in the service of offspring that are related but not its own. By so doing, the animal is protecting the genes that it has in common with those offspring. Thus, rather than being truly altruistic, such acts are actually self-serving in that they are a mechanism to protect at least some genes that are the same as the animal's. The genetic basis for the potential to act in support and defense of related offspring is thus likely to be retained in the population.

Darwin believed that the course of evolution resulted primarily from natural selection acting on variations within populations. In his view, this process produced gradual changes that could, over long periods, account for all the organic diversity that we observe today. The modern synthesis has incorpo-

rated the new knowledge of mechanisms provided by genetics, including that from the recent advances in molecular biology. Nevertheless, emphasis is still placed on the role of natural selection acting at the level of the population, as advanced by Darwin. The term **microevolution** refers to such divergences of populations within a given species, resulting in races or breeds. Microevolution involves the gradual accumulation of small changes over time, the way Darwin envisioned the evolutionary process. Another type of gradual evolutionary change is **phyletic evolution** (also called **anagenesis**). In phyletic evolution, a single lineage, without branching into divergent lineages, undergoes change over time. The ancestral and descendant portions of the lineage can become sufficiently different that they are recognized as different species.

In 1972, Niles Eldredge and Stephen Jay Gould, after examining evidence from the fossil record of marine invertebrates, pointed out that in this group at least, few examples exist of species that undergo significant change gradually through time. In most cases, a particular morphology is retained for millions of years and then changes abruptly over a short period of time. Eldredge and Gould used the term **punctuated equilibrium** to describe this pattern. Punctuated equilibrium is similar to the concept of saltatory evolution, the sudden origin of new taxa by abrupt evolutionary change, held by some of the nineteenth century biologists. The process by which new taxa are formed, from the specials level on up through the higher taxic categories, is called **macroevolution**. The formation of new species can also be referred to as **speciation** or **cladogenesis**. The term speciation is used to describe a process in which a single species gives rise to a branch that becomes established as a new, sister species or splits into two new lineages that both become new species, that is, are reproductively isolated from each other.

Darwin and a number of other biologists thought that the microevolutionary process of gradual morphological change brought about by the accumulation of genetic mutations could also explain the origin of the so-called higher taxonomic categories of species, families, orders, and classes. However, the morphological differences between various orders and families, and even those that distinguish individual species within a genus, can be considerable. After all, morphological differences are the major basis for defining these various higher categories. The new synthesis of evolution and developmental biology that is now underway reemphasizes macroevolutionary events and their crucial significance for evolutionary divergences and the formation of new taxa. Changes in the developmental process—such as **heterochrony**, a change in the relative timing of potentially related developmental events, and allometric alterations, a change in the proportional growth of a structure and/or its elements—can have dramatic effects on the phenotype. Such changes in the developmental process intervene between genotype and adult phenotype and can produce the types of substantial and rapid morphological changes that typify saltatory evolutionary events. As discussed in Box 1-1, these kinds of changes involve **developmental fields**, also called **morphogenetic fields**, **embryonic fields**, or **anlagen** (singular: **anlage**), which are the fundamental evolutionary units of macroevolutionary change. Darwin himself recognized the crucial interrelationship of embryology and evolution.

BOX 1-1. Morphogenetic Fields and the New “Evo-Devo” Synthesis

Over the past decade, it has become compellingly clear that development and evolution interact with each other, and the new synthesis occurring in biology is based on this premise. The new amalgamation of these fields of study has been dubbed “**Evo-Devo**” for short. Natural selection acts on the phenotype of the developing embryo just as it acts on the adult. The translation from the genes to the adult phenotype depends on the proper expression of the genetic instructions. Expression of various patterning genes results in expression of other genes, which in turn affect and recruit additional genes and so on, through a precisely choreographed developmental process, affecting developmental events. For example, the length of cell proliferation periods determines the number of daughter cells that form a structure and thus its volume. Whether cells of a particular set migrate to another location or remain piled up in the immediate vicinity of where they were proliferated determines the location of the structure. If the cells migrate, the order in which they do so determines their relative arrangement within the structure. All such events must occur at the proper time and to the proper degree to produce the genetically programmed phenotype. Changes in the expression levels of the patterning genes can have dramatic affects on the phenotypic outcome. Many changes can be deleterious and result in the death of the embryo, either during development or at shortly after birth. Some changes, however, can cause a substantial change in the phenotype without being lethal. Such changes, if they produce an alternate phenotype that is advantageous in terms of selective pressures, will be selected for. Major evolutionary divergences as well as lesser ones within smaller taxic groups may arise from these mechanisms.

In 1996, Scott Gilbert, John Opitz, and Rudolf Raff published a review of the new perspective that has emerged on the interplay between developmental biology and evolution. Views of homology (discussed below) and of evolutionary mechanisms are now being reevaluated, and the full biological continuum of genes-embryological development-adult phenotype is being reconciled with evolutionary mechanisms. The key to this new synthesis is the **morphogenetic field**. Gilbert et al. define morphogenetic fields as “discrete

units of embryological development . . . produced by the interactions of genes and gene products within specific bounded domains.” The fields are “modular entities [that] are genetically specified, have autonomous attributes and hierarchical organization, and can change with regard to location, time, and interactions with other modules.” Essentially, morphogenetic fields are the building blocks of development, and they interact in highly complex ways.

The expression parameters of the key patterning genes affect the morphogenetic fields and determine the variability of their products. Altering the timing of the formation of a morphogenetic field (called heterochrony) or altering other attributes of the field can affect other fields or whether the field in question is able to produce its adult phenotypic structure(s). Limb buds, for example, give rise to limbs in most vertebrates. However, in snakes, the limb buds do not produce limbs. Alteration of the properties of the limb buds results in this alteration of the normal tetrapod pattern. Thus, “the morphogenetic field (and not the genes or the cells) is seen as a major unit of ontogeny whose changes bring about changes in evolution.”

As Gilbert et al. discuss, morphogenetic fields had been a major focus of biology in the first half of the 20th century, but interest in them was eclipsed by the synthesis of genetic and evolutionary theory. The significance of morphogenetic fields has now come to be appreciated once again. Changes in them can account for saltatory, macroevolutionary events. Thus, both gradual, microevolutionary changes and the rapid, macroevolutionary changes observed in the fossil record now can be accounted for with satisfactory biological explanations.

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Evolution of the Vertebrate Central Nervous System

Extant vertebrates currently comprise diverse groups, each with diverse and numerous species. Nevertheless, in the subsequent chapters of this book, we will encounter many features of the central nervous system of vertebrates that are remarkably constant from one group to another. We will also encounter many that vary considerably. The features that are constant as well as those that are diverse have resulted from the pressures of natural selection, themselves derived from climatic and geophysical factors, acting on the randomly derived

variation in the frequency of gene alleles in interbreeding populations. Patterning genes in turn affect the morphogenetic fields, which, as discussed in Box 1-1, are the basic units of development.

Variation in the structure of the central nervous system of vertebrates has resulted from changes in the developmental program over evolution. The most salient and defining differences in brain structure and organization have resulted from alterations in the behavior of various morphogenetic fields—relatively simple changes in the length of the cell proliferation periods and the migration patterns of the neuronal precursors underlie the basic and substantial differences in organization

between mammalian brains and those of birds and reptiles, for example. Other alterations can result in the production of new cell types. Major differences within each of the major vertebrate groups as to how elaborate the brains of different taxa are also depend on proliferation and migration behaviors of various morphogenetic fields.

In a sense, the morphogenetic field is the nub of the answer to the riddle of brain evolution: complexity is most often derived from simplicity, that is, great diversity and great complexity have arisen because they both are merely the result of a few, simple random mutational events that affect the behavior of particular morphogenetic fields, the phenotypes of which have been favored highly by natural selection. Comparative neuroscience addresses the questions of how brains can change as new species evolve and how much a given part of the brain can change over evolution. To assess the variation, we first need to be able to recognize the same structures in different brains and then to compare their similarities and differences. Defining what is meant by the word “same” in this context has been an important keystone of comparative neuroanatomical analysis.

SAMENESS AND ITS BIOLOGICAL SIGNIFICANCE

Analogy

Most of this section will focus on phyletic continuity of structures across taxa and/or on the phyletic continuity of the genes and/or morphogenetic fields that produce them. The concept of **analogy** is different in that it addresses similarity of *function*, irrespective of phyletic relationships or continuity. Structures with quite different morphology, phyletic origin, and embryological origin can have quite similar functions. In other words, structures can be analogous if they serve the same function, whether they are the same or different in terms of phyletic inheritance from a common ancestor. As we will discuss below, the wing of a bird and the wing of a bat are homoplastic (independently evolved) as wings, but they are both historically homologous (inherited from a common ancestor) as forelimb derivatives and analogous as both wings and forelimb derivatives. They share the same function of flying. An elephant’s trunk and a raccoon’s hand have nothing in common phyletically or embryologically, yet they are analogous as organs for manipulating objects in the external environment. As we also will discuss for cases of both homology and homoplasy, the analogy must be specified to make sense. The wings are analogous as both wings and forelimb derivatives because they are used in the same way at both these levels. They are not analogous as feathered appendages, since bat wings have membranous surfaces rather than feathers.

Historical Homology

The concept of “same” is expressed in biology by the term **homology**. This term was first introduced by the influential British anatomist Richard Owen in 1843. Owen defined **homologue** (i.e., **homologous structures**) as “the same organ in different animals under every variety of form and function.”

Owen’s definition preceded Darwin’s theory of evolution, and modern concepts of homology have been affected by the revolutions in evolutionary biology and genetics that subsequently occurred.

Leigh Van Valen defined homology as “correspondence caused by continuity of information,” a definition that has been as criticized for its vagueness as it has been praised for its flexibility and utility. Another definition, proposed by George Gaylord Simpson, states that “homology is resemblance due to inheritance from common ancestry.” These definitions both refer to **similarity**—“resemblance” or “correspondence”—but some structures that are present in related groups of animals and that have been inherited from a common ancestor may lack any vestige of resemblance. For example, the middle ear bones of mammals (the malleus and the incus) are very unlike the articular and quadrate jaw bones of other tetrapods and from which they are ancestrally derived. Only the data provided by the fossil record allow us to recognize the common derivation of these structures.

Other definitions of homology stress **phyletic continuity**. Edward Wiley proposed that “A character of two or more taxa is homologous if this character is found in the common ancestor of these taxa, or, two characters (or a linear sequence of characters) are homologous if one is directly (or sequentially) derived from the other(s).” In this usage, the concept of homology is rooted in phylogeny. This usage can be referred to as **phyletic homology** or **historical homology**. Inheritance of the character from a common ancestor with consistent expression of the character through the various descendant lineages and across all or most members of the lineage is required to meet the definition. However, as new information accumulates and an improved understanding of the relationship of genes and developmental processes to evolutionary change is achieved, the concept of homology is changing. The newer concepts will be considered below.

A similar definition for historical homology was proposed by Michael Ghiselin: “Structures and other entities are homologous when it is true that they could, in principle, be traced back through a genealogical series to a (stipulated) common ancestral precursor.” The required stipulation is the basis of the homology. Without the stipulation, that is, **specification**, of the homology, any statement of homology is incomplete. Consider, for example, the following two statements, both of which are true:

- The wing of a bird is homologous to the wing of a bat.
- The wing of a bird is not homologous to the wing of a bat.

These two statements, although both true, are both incomplete and hence are seemingly in conflict. The wing of a bird is homologous to the wing of a bat *as a derivative of the forelimb*. The common ancestors of birds and bats possessed forelimbs of a similar basic construction, from which the wings are derived in both cases. The wing of a bird, however, is not homologous to the wing of a bat *as a wing*, since the forelimbs of the common amniote ancestors of birds and bats did not have the form of wings. Saying that A is homologous to B is as incomplete a statement as saying that “Harriet is more than Jane.” More what? More intelligent? More athletic? More sophisticated? In statements of homology, unless the specification is obvious and unmistakable, the specific characteristic being

compared must be included in the statement for the statement to be meaningful.

Several different types of historically homologous relationships can be recognized. Hobart Smith gave clear and concise definitions of them in his 1967 paper on biological similarities. The most common type might be called a **discrete homology**, defined as "common ancestry of structures which can be compared individually. . . ." Alternate terms for discrete homology are **strict homology** or **one-to-one homology**. The wing of a bird being homologous to the wing of a bat as a forelimb derivative is an example of a discrete homology, in that a discrete structure in each of two or more taxa is being compared. Additional types of homology, as specified by Smith, are also applicable to neuroanatomical studies. A **serial** or **iterative homology** (also called homonymy) involves structures that are derived from the same ontogenetic division of two or more segments in a single individual organism, such as the wing of a bird and the leg of the same individual bird, as serially derived tetrapod limbs. Vertebrate ribs, vertebrae, and spinal cord segments are additional examples of serial homology. Also involving development is the concept of **field homology**, which applies to structures that are derived from the same ontogenetic source, i.e., the same morphogenetic field (see Box 1-1), across taxa. An example of a field homology is the five digits of a human hand being homologous as a set of derivatives of a common morphogenetic field to the set of the lesser number of distal forelimb divisions in a variety of other mammals. The topic of field homology is discussed further in Box 1-2.

Since the features of any given structure may be altered in different lineages, fossil evidence has played a significant role in identifying homologous parts of the musculoskeletal system among vertebrates. The brain does not fossilize, however, so other criteria for proposing hypotheses of historical homology are needed for neuroanatomical work. These criteria are based on the degree of similarity and were proposed by Simpson in 1961. They include the **minuteness of the resemblance** and the **multiplicity of the similarities**. In neuroanatomical studies, the features that can be compared for a given group of neurons in two different extant taxa include:

- Topological similarity.
- Topographical similarity.
- Similarity of axonal connections.
- Similarity in their relationships to some consistent feature of the two species.
- Similarity of embryological derivation.
- Similarity in the morphological features of individual neurons that form the group.
- Similarity in the neurochemical attributes of the neurons.
- Similarity in the physiological properties of the neurons.
- Similarity in the behavioral outcomes of neuronal activity.

Not all of these criteria can be met in every case. Some would argue strongly against including the last two criteria, noting that comparisons should be structural only and never functional. Nevertheless, the more of these criteria that can be satisfied, the stronger the support for an hypothesis of historical homology, that is, phyletic continuity. In those cases in which structures that are homologous also meet most or all of

the above criteria for similarity, the term **homogeny**, or its adjective **homogenous**, can be applied, although these terms are rarely encountered in the literature.

Homoplasy

Homoplasy is the opposite of historical homology. The term is used to refer to structural similarity without phyletic continuity, and its adjective is **homoplastic**. Structural similarity can occur in divergent lineages as a result of similar adaptive responses to similar environmental pressures rather than as an inheritance from ancestors. The wing of a bird and the wing of a bat are not homologous as wings; they are homoplastic as wings. Note again that the relationship must be specified to make sense. Structural similarity without phyletic continuity can also result from changes in the expression of particular patterning genes, with alterations in the fate and behavior of morphogenetic fields.

Three different types of homoplasy are recognized: **convergence**, **parallelism**, and **reversals**. Convergence refers to the process of similar responses to similar adaptive pressures, but the responses are based on entirely different genes and morphogenetic processes. Convergence has been defined by Wiley as "the development of similar characters from different preexisting characters." Convergence usually occurs in remotely related animals, and the degree of similarity and the minuteness of the resemblance are limited and generally superficial.

Parallelism, in contrast, usually occurs in closely related taxa, and the degree of similarity and minuteness of the resemblance tend to be extensive. Wiley defined parallelism as "the independent development of similar characters from the same plesiomorphic [i.e., ancestral] character." In other words, the descendant character is not present in the common ancestor of two taxa, but each of the descendant taxa develops the descendant character after the time of their evolutionary divergence. One implication of parallelism is that the genetic and/or morphogenetic material that produces the structures in the different taxa is the same, i.e., inherited from a common ancestor with phyletic continuity. In both homology and parallelism, similar structures are present in closely related animals with similar survival problems that have adapted in similar ways. Historical homology differs from parallelism only in the consistency with which the structure is phenotypically expressed along the phyletic lineage or across the phylogeny of extant taxa.

When such instances of similar structures being present in closely related species occur, distinguishing between parallelism and historical homology can sometimes be difficult. In these circumstances, assuming historical homology is regarded as the preferable tactic. The German scientist Willi Hennig codified this method in his **auxiliary principle**: "Never assume convergent or parallel evolution; always assume homology in the absence of contrary evidence." As we will discuss below, this method is based on the idea that it is simpler for a common ancestor to acquire a given structure once than for each of two descendent groups to acquire it independently. Also, the biological basis for the structure is the same for historical homology and parallelism. For understanding evolutionary processes, identifying shared genetic and morphogenetic bases of structure is more important than distinguishing between historical homology and parallelism. Tables 1-1 and 1-2 offer

BOX 1-2. Field Homology

Field homology involves structures that are embryologically derived from the same developmental field. In a 1967 paper, Hobart Smith defined it as “derivation of structures, however similar or dissimilar, from a common anlage, or in other words, from the same ontogenetic source of the same or different segments, of any two or more compared individuals or groups of individuals.” Interestingly, Smith recognized the seminal importance of embryology for the concept of homology; he defined homology itself as “commonness in phylogenetic *or embryonic* origin of two or more specific compared structures, irrespective of similarity of structure or function [our italics].”

The concept of field homology rests on the concept of the developmental, or morphogenetic, field itself (see Box 1-1). With the new, “evo-devo” synthesis and the rediscovered appreciation of the morphogenetic field, the legitimacy of the field homology concept has been accepted by a number of comparative neurobiologists. For a field homology to be valid, it is required that the morphogenetic fields themselves be homologous, either historically or as defined by evo-devo perspectives (as discussed below).

It is important to note that the field homology concept is generally used to compare a set of derivatives in the adult phenotype in one taxon with the corresponding set of derivatives in the adult phenotype of another taxon. It is not appropriate to make “diagonal” comparisons of noncorresponding developmental stages in two different taxa. In other words, the comparison should be “horizontal,” as across the rungs of a ladder, with the side rails representing time and each rung connecting comparable developmental stages. That is to say, homologous morphogenetic fields need to be compared at similar stages of their development rather than comparing an early stage in one taxon to a later and more differentiated field in another taxon. Glenn Northcutt has argued against the use of the morphogenetic field homology concept, partly on the basis of improper “diagonal” comparisons, and this point is a crucial one, since one must try to distinguish between homologous field derivatives and the appearance of a truly new structure—an **evolutionary innovation**.

In Figure 1, Northcutt’s diagram is shown in A, which shows three taxa descended from a common ancestor. This common descent applies to the examples shown in B and C as well. In A, two structures, E₁ and E₂, have developed in Taxon 3 as derivatives of an additional developmental stage that has no homologue in Taxa 1 and 2, i.e., the E morphogenetic field that produces E₁ and E₂ is not homologous to the D field of Taxa 1 and 2. The field homology concept, as currently applied by others, would also invalidate this comparison. It would require that a homologous morphogenetic field E be identified in Taxa 1 and 2 for the comparison of derivatives to be valid, as shown in the example in B. In both A and B, it is implied that E developed from D, but another possibility, that of evolutionary innovation, must also be considered, as shown in the example in C. In this

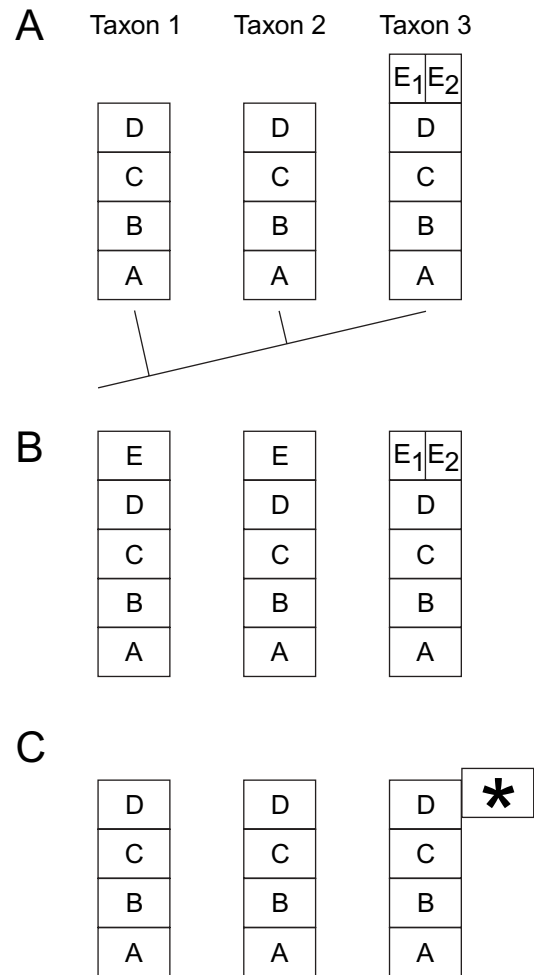


FIGURE 1. Examples of successive stages in the development of a morphogenetic field in three taxa. (A) after Northcutt (1999) showing noncomparability of E₁ and E₂ in Taxon 3 to D in Taxa 1 and 2. (B) correct field homology hypothesis of E₁ and E₂ in Taxon 3 to E in Taxa 1 and 2. (C) evolutionary innovation, indicated by * in Taxon 3, which is not derived from D and must be excluded from comparison with the derivatives of D among all three taxa.

situation, an entirely new, autonomous morphogenetic field, indicated by the asterisk, enters the picture in Taxon 3, which is independent of the temporal series of development of the field A-B-C-D-(E) in Taxa 1 and 2. Such a scenario is illustrated by distal limb development in tetrapods (Taxon 3 in this example), as Günter Wagner and Chi-hua Chiu have discussed. This diagram oversimplifies the actual history of tetrapod limb evolution (see Chapter 7), but the point to be made here is that a new component, produced by a new morphogenetic field, cannot be included in the set of deriv-

BOX 1-2. Field Homology—cont'd

atives of another field, D, and then compared to the derivatives of D in another taxon. In other words, one must be precise in determining the derivatives of any given morphogenetic field for a hypothesis of field homology to be valid. This point is of particular importance for illuminating the evolution of various parts of the brain across vertebrates.

It should also be noted that, although development from a common morphogenetic field is an important criterion for recognizing homology, it is not absolute. Other criteria must also be weighed. While most historical homologues arise from historically homologous morphogenetic fields, some arise from nonhomologous fields. Such exceptions are few but do occur. The lens of the eye, for example, can be derived from different sources.

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TABLE 1-1. Comparisons With a Human Hand

Basis of the Relationship	Hand of a Monkey	Hand of a Raccoon	Forepaw of a Rat	Wing of a Bat	Wing of a Bird	Wing of a Moth
Historically homologous as a hand?	Yes—their common ancestor had hands	No—their common ancestor had forepaws, not hands	No—their common ancestor had forepaws, not hands	No—their common ancestor had forepaws, not hands	No—their common ancestor had forepaws, not hands	No—an insect wing is not related to a hand
Homoplastic as a hand?	No—they are historically homologous	Yes—it looks roughly like a human hand	Yes—in some respects but not to the same degree as in the case of the raccoon	No—it does not resemble a human hand	No—it does not resemble a human hand	No—it does not resemble a human hand
Historically homologous as a forepaw?	Yes	Yes	Yes	Yes	No—bird wings are forelimbs, not forepaws	No—an insect wing is not related to a forepaw
Homoplastic as a forepaw?	No—they are historically homologous as forepaws	No—they are historically homologous as forepaws	No—they are historically homologous as forepaws	No—they are historically homologous as forepaws	No—bird wings are forelimbs, not forepaws	No—an insect wing does not resemble a forepaw
Analogous?	Yes—used for manipulation	Yes—used for manipulation	Yes—used for manipulation	No—used for flight, not manipulation	No—used for flight, not manipulation	No—used for flight, not manipulation

some opportunities to see whether you understand the differences between historical homology, homoplasy, and analogy. They also point out the importance of specifying the relationship.

Reversals are instances of a character appearing, subsequently disappearing, and still later reappearing along the descendants in one lineage. Since the character is not consistently expressed in the phenotype, it cannot be considered to be historically homologous. Because most and perhaps all cases of reversal are based on expression of the same underlying gene and/or morphogenetic field and processes, inherited

down the lineage from the common ancestor, they are closely related to parallelism.

Biological Homology

A number of other approaches to homology have been taken by various scientists. The historical homology concept does not satisfy some situations, due to its failure to recognize the importance of genetic and morphogenetic continuity as the bases for sameness. Its insistence on consistent phenotypic expression of a particular character in all or most members

TABLE 1-2. Comparisons With an Eagle's Wing

Basis of the Relationship	Wing of a Sparrow	Wing of a Crow	Wing of a Bat	Wing of a Moth
Historically homologous as a wing?	Yes—their common ancestor had wings	Yes—their common ancestor had wings	No—their common ancestor did not have wings	No—their common ancestor did not have wings
Homoplastic as a wing?	No—they are historically homologous	No—they are historically homologous	No—it does not resemble a bird wing	No—it does not resemble a bird wing
Historically homologous as a forelimb derivative?	Yes	Yes	Yes	No—an insect wing is not related to a forelimb
Homoplastic as a forelimb derivative?	No—they are historically homologous	No—they are historically homologous	No—it does not resemble a bird wing	No—an insect wing does not resemble a forelimb
Analogous?	Yes—used for flight	Yes—used for flight	Yes—used for flight	Yes—used for flight

of a taxon is at odds with biological reality, which includes cases of inconsistent phenotypic expression. Two alternative approaches discussed here are **biological homology** and **generative homology**, or **syngeny**. One could say that, although historical homology focuses on phyletic continuity, biological homology focuses on morphological identity, and generative homology focuses on genetic and morphogenetic identity. These concepts are not mutually exclusive. In fact, they overlap considerably. These concepts are each best suited for a different research interest—historical homology for phylogenetics and systematics, biological homology for character evolution, and generative homology for comparative developmental biology.

Biological homology is an alternative approach that addresses how characters evolve and become stabilized within a taxon and the mechanisms of character evolution. Biological homology focuses on developmental pathways and the behavior of morphogenetic fields to account for variability of character expression but does not define sameness by them. It attempts to link historical homology to developmental processes and constraints. Biological homology was defined by Leigh Van Valen in 1982 as “resemblance caused by a continuity of information” and by Louise Roth in 1984 as based on “sharing of pathways of development . . . controlled by genealogically related genes.” In 1989, Günter Wagner stated that “Structures from two individuals or from the same individual are homologous if they share a set of developmental constraints, caused by locally acting self-regulatory mechanisms of organ differentiation. These structures are thus developmentally individualized parts of the phenotype.” This concept of homology seeks to understand why individualized parts of the body behave as units that maintain their structural identity. Gerd Müller and Günter Wagner more recently defined biological homology as “the establishment and conservation of individualized structural units in organismal evolution.” Most if not all cases of biological homology are also cases of historical homology.

Generative Homology or Syngeny

A number of approaches to the problem of parallelism have been taken, including the concepts of **latent homology**

put forward by Gavin deBeer in 1971. He proposed that this term should refer to characters that occur within only some members of a taxon but that may not have been expressed in the common ancestor and are not expressed in a substantial number of the other members of the taxon. Other similar concepts have been put forward, but they have focused on parallelism (and reversals) rather than addressing the close relationship of historical homology to these phenomena.

The discovery of a particular cell group in the brain of teleost fishes prompted Ann Butler and William Saidel to scrutinize current concepts of homology and to propose a new concept—that of generative homology, or syngeny. The cell group in question, nucleus rostrrolateralis, will be discussed in Chapter 21. This nucleus has a very sporadic and far-flung phylogenetic distribution within ray-finned fishes, and it is absent in many taxa that are in phylogenetically intermediate positions to those where it occurs. Nevertheless, where present, it has many and minute similarities. It is an example of very distant parallelism, due to inconsistent expression of its underlying genetic and morphogenetic bases. This unusual pattern of expression of what is clearly the “same” nucleus was the impetus for reexamining the issues of homology and for formulating the concept of generative homology, or syngeny.

The term syngeny means “same genes,” since the concept addresses the issue of phyletic continuity of genes and morphogenetic pathways and fields rather than of the adult phenotype per se. Generative homology is closely allied to biological homology, but it specifically states that the recognition of sameness is based on shared genetic/morphogenetic pathways that are inherited with continuity across the members of a taxon. Whether expression of the character is consistent (historical homology) or inconsistent (parallelism or reversals) is not of importance in recognizing the biological relationship of sameness. Thus, generative homology comprises parallelism, reversals, and most cases of historical homology. It is a unifying concept that separates these three phenomena from convergence. The latter is referred to as **allogeny**, meaning “different genes.”

The historical homology/homoplasy conceptual stance divides characters along artificial lines with its insistence on

TABLE 1-3. Historical Homology Versus Generative Homology

	Components	Biological Basis	Phenotypic Expression	Opposite
Historical Homology	Historical homology cases only	Inheritance from common ancestor of the character itself	Required to be consistent along and/or across the taxon	Homoplasy: parallelism, reversals, and convergence
Generative Homology	Most cases of historical homology plus parallelism and reversals	Inheritance from common ancestor of genetic and/or morphogenetic basis for the character	Can be either consistent or inconsistent along and/or across the taxon	Alloeny (= convergence)

consistent phenotypic expression. The syngeny/alloeny conceptual stance recognizes that historical homology, parallelism, and reversals all share the inherited underlying genes and morphogenetic processes and thus form a natural conceptual group. Convergence, similarity due to different, noninherited genes and morphogenetic processes, stands alone as the opposite phenomenon. The difference in these two concepts is highlighted in Table 1-3.

The generative homology concept will be of particular relevance in dealing with the plethora of recent findings on patterning genes and the stunning similarity of their expression patterns in some taxa of bilaterally symmetrical animals. As we will discuss further in Chapter 31, many of the same genes that specify basic developmental events in vertebrates, including those for the central nervous system, also occur in invertebrates and have the same roles. Many of the genes that specify the basic divisions of the brain and the formation of the eye, for example, are the same in fruit flies and mice. In such cases, the word “homology” is sometimes used. However, because the common ancestor clearly did not possess a comparable brain or eyes, these structures in mice and flies cannot be historically homologous. Nonetheless, even their designation with the same words, “brain” and “eye,” denotes recognition of a basic level of sameness, and, as products of the same patterning genes that were present in the common ancestor, they are indeed the same. The brains of flies and mice as whole brains and the eyes of flies and mice as whole eyes are examples of generative homology; they are **syngenogues** to the extent that they are products of the same set of genetic and morphogenetic processes.

ANALYSIS OF VARIATION

Recognizing similar structures present in different taxa is the first part of the process of reconstructing evolutionary history, which, in the absence of a corroborating fossil record—as is the case with most features of the central nervous system—is essentially a guessing game. Although we may come up with sophisticated theories that seem to account for the data, there is no guarantee that these theories are correct. This is a problem that exists in many areas of science, such as astronomy, geology, psychology, and economics, to name a few. An approach to evolutionary reconstruction of the central nervous system that has been used with considerable success is a methodology called **cladistics**.

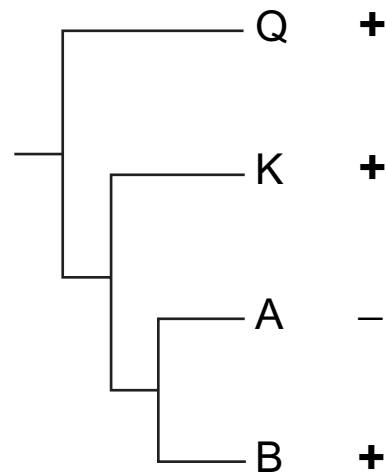


FIGURE 1-1. Cladogram showing the distribution of a trait, indicated by +, among the theoretical extant taxa Q, K, A, and B.

Cladistic Analysis

Cladistics is a formal method of analysis for classifying animals according to their inferred phyletic relations, based on sets of shared similar traits. This approach is the embodiment of the historical homology concept. It can be applied to analyzing the variable occurrence of a given trait among different taxa. In the latter case, a highly corroborated hypothesis of phylogenetic relationships of the taxa under consideration is needed. This phylogenetic hypothesis should be one that is derived from sets of traits not related to the trait being analyzed and also is based on a large number of such traits. It is usually structured in the form of a **cladogram** or **dendrogram**, that is, a tree-like diagram of the species representing their genealogy, produced using cladistic methods of inference. For example, hypotheses of phylogeny, such as those presented in Chapter 4 and based predominantly on fossorial and osteological data, are appropriate to use in the analysis of the distribution of central nervous system traits. Traits that are **plesiomorphic**, that is, are similar to those present in a particular ancestral stock, need to be distinguished from traits that are **apomorphic**, that is, derived specializations within a particular taxon.

The observed distribution of the trait to be analyzed is plotted on the terminal branches of the cladogram, an example of which is shown in Figure 1-1. The pattern of distribution of

the trait in various ancestral groups that can account for the observed distribution in the living (terminal branch) taxa via the *fewest* number of phylogenetic transformations is then inferred. This process thus generates an hypothesis about the evolutionary history of the trait based on its distribution in extant taxa. In our example (Fig. 1-1), we are considering four taxa: A, B, K, and Q. All are descended from a common ancestral stock, but A and B are more closely related to each other than to K. Also, the taxon K and the group of A and B are more closely related to each other than to Q. Taxon B has a particular trait, indicated by the + sign, but the related taxon A does not. Did the common ancestor of A and B have the trait, with the line leading to A subsequently losing it, or did the common ancestor lack the trait and the line leading to B alone gain it?

Cladistic analysis uses **out-group comparisons**, that is, comparisons of the trait in sister taxa, which are taxa more closely related to the taxon being studied than to any other taxon. In our example, we thus first examine taxon K, the out-group, or sister taxon, to the group of B and A, for the presence or absence of the trait and find that it is present in K. One possible scenario, which would require two transformations, is that the trait was gained at some point in the common ancestor of K, A, and B (transformation 1) and was subsequently lost in A (transformation 2). The alternative scenario is equally likely, since it would also require two transformations—the absence of the trait in the common ancestor with its independent gain in K (transformation 1) and B (transformation 2). Thus, on this information alone, we cannot decide which possibility to choose for our working hypothesis. To resolve the question, we can examine taxon Q, the out-group to K, A, and B. We find that the trait is present in Q. Thus, the scenario with the least transformations is that the trait was acquired in the common ancestor of all these taxa (transformation 1) and was subsequently lost only in A (transformation 2). This hypothesis requires fewer transformations than the alternative of three independent acquisitions of the trait in Q, K, and B. It also requires fewer transformations than the other alternative scenario of absence of the trait in the common ancestor, its gain in Q (transformation 1), its independent gain in the common ancestor of K, A, and B (transformation 2), and its subsequent loss in A (transformation 3). Cladistics thus provides a rigorous method for inferring the likely nature of structures in common ancestors and, therefore, which structures are plesiomorphic (ancestral) and which are apomorphic (derived).

Could an alternate scenario to the one with the least transformations actually have occurred? Of course! That is why it is so crucial to employ the scientific method of continually challenging and testing hypotheses. Also, the more taxa that one can examine for the presence or absence of a trait, the less likely is the possibility of error in formulating the hypothesis. It is also why the principle of parsimony serves us well.

Parsimony

Generating an hypothesis of historical homology based on the smallest number of phylogenetic transformations is in accordance with the **principle of parsimony**. In its simplest form, this principle states that if one is confronted by several competing theories or explanations, the simplest one (or the

one with the fewest assumptions) is most likely to be correct. Please note that the principle states the simplest explanation is *most* likely to be correct. Parsimony is no guarantee of correctness. In biology, nonetheless, simple explanations seem to be supported by subsequent facts more often than more complex explanations. In the case of the distribution of a trait in Q, K, and B but not A, as shown in Figure 1-1 for example, we would have no grounds to assume that if the common ancestor of A and B had the structure, then a subsequent ancestor of A lost it, another subsequent ancestor of A regained it, and yet another subsequent ancestor lost it again. Unless there were specific evidence to support this having happened, most biologists would find such an elaborate hypothesis to be quite unconvincing. Hence, the value of parsimony: it tends to rule out overly elaborate hypotheses, which is a justified result in most cases. The more elaborate hypothesis described in this example, however, would be a case of reversal, which, as noted above, refers to the gain, loss, regain, and so on of a trait subsequently along a lineage through time. Reversals, although not frequent, do occur, and the cladistic method is not well suited to reveal them.

The principle of parsimony is in accord with current ideas about the mechanisms of evolution for most situations. Any given species does not have a good chance of success if it gains new traits that do not give it an advantage in maintaining itself or if it loses traits that were beneficial to survival. If a new trait allows for a new niche or adaptive advantage, the trait will be selected for and maintained in the phenotype. Most, but not all traits, fit this model. Also in most cases, changes in the genome conform to the principle of parsimony. The simpler the alteration of the genome to produce a variant, on which natural selection can then act, the greater the probability of its occurring and becoming established in a population. This is the **principle of minimum increase in complexity**, as delineated by Peter Saunders and Mae-Wan Ho.

Let us extend our example of using the principle of parsimony in an **out-group analysis** by analyzing the variation of a hypothetical trait with some real taxa, as shown in Figure 1-2, in order to better demonstrate the correct method of analysis and the importance of being rigorous in applying it. Figure 1-2 shows a somewhat simplified cladogram of the major taxa in the vertebrate radiation (which will be discussed in Chapter 4). A plus sign is placed to the right of each taxon where the trait is present and a minus sign where it is absent. We first note that the trait is present in the amniote vertebrates—mammals, reptiles, and birds—but is absent in amphibians. Was it present or absent in the common ancestor of amphibians and amniotes? The out-group to amphibians and amniotes, that is, tetrapods, is the crossopterygian *Latimeria*, and in our example, *Latimeria* lacks the trait, as do the lungfishes. We therefore hypothesize that the trait was absent in the common ancestor of lungfishes, *Latimeria*, and tetrapods. This would mean that only one transformation occurred over evolution among these groups: the acquisition of the trait in the ancestral stock of amniotes. We can also conclude that the trait was not acquired in the common ancestor of tetrapods, because such a change would then have to be followed by another change (the loss of the trait in extant amphibians), and this scenario is not parsimonious. Two changes are more complicated than one, so the hypothesis of two changes must be discarded.

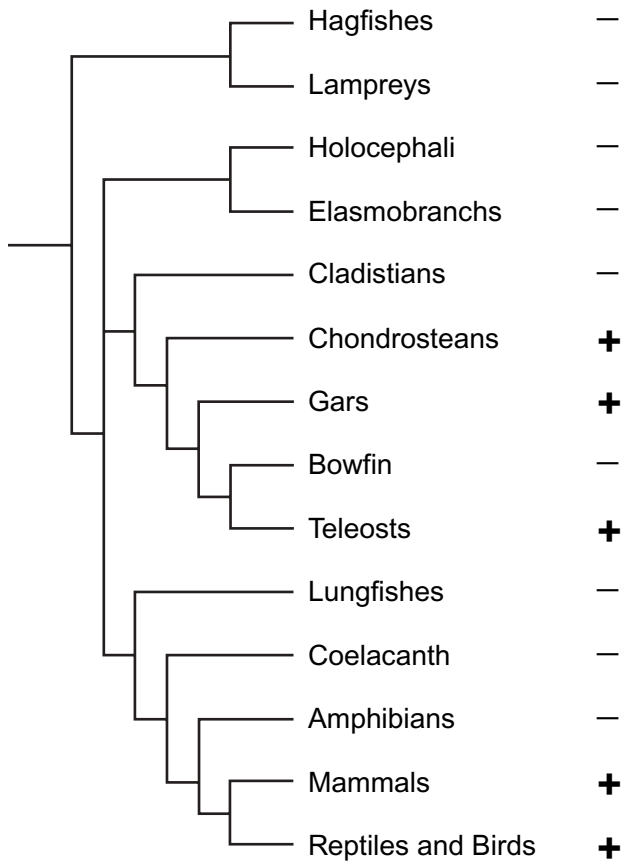


FIGURE 1-2. Cladogram showing the distribution of a trait, indicated by +, among extant groups of vertebrates. (The groups themselves will be discussed in Chapter 3.)

We now turn to the ray-finned fishes and find that a similar trait is present in teleosts, absent in the bowfin, present in gars and chondrosteans, and absent in cladistians. Comparing only teleosts and the bowfin, we do not know whether the trait was present or absent in their common ancestor. Gars and chondrosteans are the out-groups to the bowfin and teleosts, and they have the trait. Therefore, we hypothesize that the trait was present in the common ancestor of these four groups and that it has been lost once—in the bowfin. The trait is absent, however, in cladistians. Was it present or absent in the ancestral stock of ray-finned fishes? The out-group to the ray-finned fishes is the cartilaginous fishes, and the trait is absent in both groups of cartilaginous fishes—holocephali and elasmobranchs. Thus, we hypothesize that the trait was absent in the common ancestors of cartilaginous and ray-finned fishes. It was gained in the ancestral stock of chondrosteans, gars, the bowfin, and teleosts and was subsequently lost in the bowfin.

Jawless vertebrates (hagfishes and lampreys) also lack the trait, so we can extend and summarize the above hypotheses to the following: the trait was absent in ancestral vertebrates, was gained once in the common ancestral stock of chondrosteans, gars, the bowfin, and teleosts (transformation 1), was lost in the bowfin (transformation 2), and was independently gained a second time in amniotes (transformation 3).

Three is thus the minimum number of changes that can satisfy this distribution. If, on the other hand, we were to ignore parsimony and hypothesize that the trait was gained in the ancestors of ray-finned fishes and then lost in reedfishes, in the bowfin, in the coelacanth, in lungfishes, and in amphibians, we would have to ascribe to six transformations, twice the number that accounted for the pattern in the more parsimonious hypothesis.

Using the principle of parsimony has important implications for distinguishing historically homologous structures from homoplastic ones. Given the distribution of the trait in our example, we must conclude that the trait in some of the ray-finned fishes and the trait in the amniotes are homoplastic and not historically homologous, even if they resemble each other closely. If two structures are homoplastic, we can examine to what degree they are similar and assess what constraints may be operating and how much potential exists for the development of new structures over evolution. If multiple and minute resemblances exist between structures in phylogenetically far-flung taxa, a hypothesis of generative homology would be justified, as in the case of nucleus rostralis discussed above. Again, the homology must be specified. For example, the eyes of fruit flies are generatively homologous to the eyes of mammals as whole eyes engendered by a specific set of patterning genes. They are not generatively homologous at a finer morphological level, since the ommatidial units of the fly eye are specified by different genes than the mammalian retina and are very different in structure.

Tests of Homology

In 1982, Collin Patterson published an influential paper on homology, in which he noted three different types of homology generally recognized at that time, including historical homology. In this paper, he offered a set of three tests that could be applied to any question of homology. These tests stand today as highly useful for evaluating hypotheses of homology—historical, biological, or generative. The first test is that of similarity. This has been discussed above. Most homologous structures show evidence of similar features, including developmental, topological, and morphological ones. The second test is that of congruence, which specifically applies to cases of historical homology. It specifies that the character in question be distributed in a pattern that is congruent with another, unrelated synapomorphy (advanced character). The third test, which we have not yet discussed, is a useful one to keep in mind. It is the test of **conjunction**, which states that “If two structures are supposed to be homologous, that hypothesis can be conclusively refuted by finding both structures in one organism.” For example, if a particular neural cell group in one organism is proposed to be homologous to a certain neural cell group in another organism, finding the latter cell group to be present also in the first organism would nullify the hypothesis.

A Word of Caution

We need to return to the example shown in Figure 1-2 to consider one last important point. A major pitfall can arise when using cladistic analysis that we need to be aware of. This pitfall involves ignoring the presence of out-groups to

the assemblage being examined. If one of the more so-called "advanced" members of a taxon (i.e., those that are farther or more recently derived from the ancestral stock than others) differs from an extant species that is more closely related to the ancestral stock, one may be tempted to make the mistake of taking the condition in the latter species as the ancestral condition. Statements that reveal this line of thinking unfortunately appear with some frequency in scientific journals.

If we return to Figure 1-2 and consider the absence of the trait in reedfishes, the potential pitfall in logic can be appreciated. We concluded, since the trait is absent in cartilaginous fishes and agnathans, that the trait was also absent in the common ancestor of ray-finned fishes and was not acquired in this line until after the divergence of cladistians from the rest of the taxon. In this case, the absence of the trait in cladistians does mirror the ancestral condition. Had the trait been present in cartilaginous fishes, lampreys, and hagfishes, however, we would have concluded that the trait was present in the common ancestor of all vertebrates and thus also present in the ancestral stock of all ray-finned fishes. In this case, its absence in cladistians would be a *specialization* within that group, as is the case in bowfins.

One of the most important concepts to bear in mind in comparative analyses is that while traits can be plesiomorphic or apomorphic, a particular species is neither. Any species is the sum of its traits—some of which are plesiomorphies and some of which are apomorphies. The position of any species on any type of phylogenetic tree does not have any correlation with the presence or absence of primitive or derived traits.

Reconstructing Evolution

The results of cladistic analyses can give us a picture of the various traits possessed by a particular ancestral group. In comparative neurobiology, we can thus reconstruct the neuroanatomical features in an ancestral stock and then compare them with the sets of features found in the various descendant, extant groups of that stock. Being able to identify the differences then allows us to formulate hypotheses about the mechanisms of how the evolutionary changes came about. For example, could the difference between one condition in an ancestor and a different condition in a descendant be accounted for by differences in the rate of cell proliferation during development? By a different migration pattern of neurons during development? By a lack of afferent axonal connections resulting in loss of a group of neurons during development?

In reconstructing the condition of the central nervous system in ancestral groups, we can thus gain a foothold on the challenge of finding out *how* brains have evolved. As many of the chapters in this book will demonstrate, the various parts of the brain have some very different evolutionary histories in different lineages of vertebrates. In all cases of extant vertebrates, the evolution of the brain has allowed for the particular species to be successful in its adaptation to its environment.

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2

Neurons and Sensory Receptors

INTRODUCTION

Virtually all animal cells react in some way to the physics and chemistry of the environments that they inhabit. Some multicellular animals, however, have evolved a special network of cells (neurons) that have the ability to communicate with specific groups of other neurons in a highly precise manner. This cellular communication network is the nervous system. Among the advantages of a nervous system are that it is able to take information about the surrounding environment and process it in some way before the animal reacts. This processing provides the animal with options such as to respond or not respond to a stimulus, or to respond one way or another way. In addition, a nervous system offers the ability to store information about the consequences of a particular response to a particular environmental stimulus; this information can then have an impact on the course of future action when a similar stimulus next occurs. Because of the wide range of chemical and physical events that are of importance to animals, certain neuron or neuron-like cells became specialized for the detection of these stimuli, such as light, pressure, chemical, and temperature detectors. These nervous system specializations, known as receptors, along with specializations of various body parts, permitted animals to enter and exploit new regions of the environment. To the extent that these explorations were successful, they led to further specialization and adaptation.

In this chapter we will examine some of the fundamentals of the anatomy of neurons and receptors as individual elements of the nervous system. In subsequent chapters we explore the organization of these elements into neuronal systems. Among these systems are:

- Sensory systems that acquire information about the external and internal environments.
- Integrative systems that process the incoming information, evaluate this information, often in the context of past experience, and make decisions for action or inaction, depending on the circumstances.
- Motor systems that convert decisions into commands for action (or inaction) by effector organs (muscles and glands).
- Coordinating systems that organize the patterns of commands to the effector organs, especially muscle groups, to assure that the individual effector organs or groups of organs operate on the environment in a smooth, efficient, and orderly way.

THE NERVOUS SYSTEM

The nervous system, like all organs of the body, is made up of cells. Like many organs, the nervous system contains more than one specialized type of cell. Unlike other systems of the body, however, the nervous system has a great variety of cell types and sizes arranged in highly specific ways, which are fundamental to its operation. Indeed, these highly specific relationships between its cellular constituents are what give the nervous system its unique character, which permits us to have automatic central control over our internal organs, to sense the external and internal environments, to remember, to think, to communicate, and so on. These functions depend on precise interconnections between specific cell populations. In no other biological system does the functioning of that system depend on such precise and rapid communication between

one particular cell and another. Moreover, the sequences in which the cells communicate are fundamental to the way in which the nervous system functions. If, for example, these relationships are interfered with by injury, disease, or developmental malformation, important visceral and behavioral functions that the nervous system performs will be impaired.

Another major difference between the nervous system and other organs is the distance over which many of the cellular components communicate. In large animals such as humans, whales, elephants, and giraffes, the distances over which a single neuron communicates with other neurons can be a meter or more. In addition, in these large creatures, the lengths of the cells that carry information from the body surface to the nervous system and those that carry the nervous system's commands to the muscles can be many meters in length.

The cells of the central nervous system fall into two broad categories: **neurons** and **glia**. The neurons are the communication and information-processing elements of the nervous system. The glia are support elements; they protect and nurture the neurons and may play a subtle role in the processing of information. In addition to its cells, the nervous system contains a rich supply of blood vessels to bring oxygen and nutrients to the cells and to remove waste products.

Neurons communicate with each other by means of signals that are mostly chemical, sometimes electrical, and occasionally a mixture of the two. When the communication must be carried out at a distance, the transmission of the signal along the length of the neuron is carried out by means of an electrochemical process known as the nerve impulse or action potential. Because so much of the mechanism of transmission of the signal from cell to cell is by means of the rapid secretion of chemicals into the minute space between cells, neurons may have evolved from secretory cells that became specialized for secretion to one particular cell rather than to any cells that happen to be in its vicinity. As the nervous system grew in size and neurons became spatially separated, they developed the capability to maintain their specific-cell-to-specific-cell contacts over longer and longer distances.

Because the nervous system is the organ of behavior, it must acquire information about the external world and the condition of internal organs and systems. This information is acquired by means of specialized cells called **sensory receptors**. Many receptors are specialized neurons; others are neuron-like cells that have a number of properties in common with neurons and are innervated by neurons that relay the sensory signals to the central nervous system.

The following sections contain a brief description of some characteristics of neurons and receptors that will be especially useful for readers of this book. We assume that the reader already has a basic familiarity with the structure of neurons, their component parts, and the basic principles of axonal conduction and synaptic transmission. Readers who lack this background or wish to refamiliarize themselves with it will find a separate listing of introductory works on these subjects at the end of this chapter.

NEURONS AND SENSORY RECEPTORS

The main components of the neuron are the cell body, or **soma**, and its processes or outgrowths: the **axon** with its axon

terminals and the **dendrites** with their dendritic branches and spines. Each of these components can be found in a seemingly endless variety of configurations. Figure 2-1 shows three examples from the wide variety of neuron types. In each of the examples, the arrows indicate the direction of flow of the nerve impulse. The motor neuron shown in Figure 2-1(A) shows the main components of neurons. The star-shaped, solid black region represents the soma, which consists of a cell membrane that contains cytoplasm and the **nucleus**.

The large extensions or processes that give the soma its star shape are the dendrites. The dendrites themselves may have further processes extending from them and are known as dendritic branches. These branches in turn often subdivide further into smaller and smaller branches until they take on the appearance of a leafless tree in winter. The soma and its dendritic tree are the most frequent points of contact between a neuron and those other neurons that are sending their communication signals to it. The size and shape of the soma can vary enormously among neuron types. The soma may be as small as a few micrometers to more than a millimeter, as in the giant cell of Mauthner, which is discussed in Chapter 8. It may be star shaped, as in the example, or it may have many other forms, such as that of a pyramid (pyramidal cell), a pear (piriform cell), or a spindle (fusiform cell), examples of which are shown in Figure 2-3. Dendrites can vary in length from a fraction of a micrometer to many millimeters.

Also projecting from the soma is the axon, which is the component of the neuron that permits long-distance communication. Often axons also are referred to as "nerve fibers" or simply "fibers." In this book, we will use the terms axons and fibers interchangeably. The axon leaves the soma from a gentle swelling called the axon hillock and travels over distances that

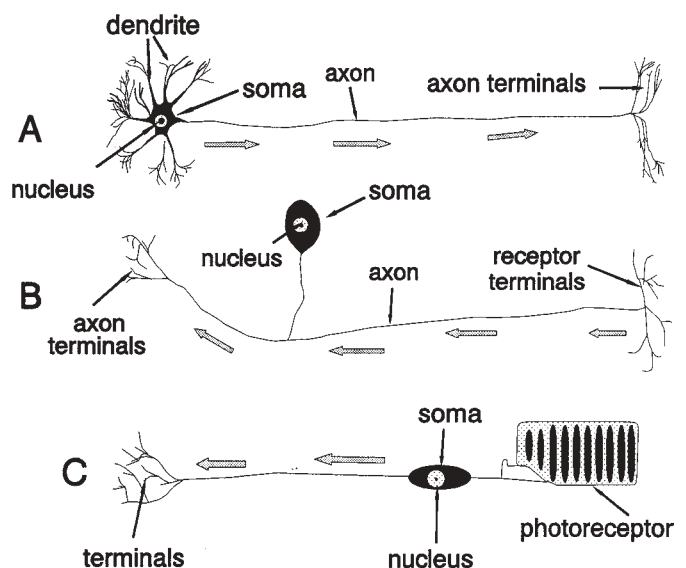


FIGURE 2-1. Examples of three types of neurons. (A) A typical motor neuron with a roughly star-shaped soma, dendrites, axon, and axon terminals. (B) A typical sensory neuron with a pear-shaped soma that is separated from the axon by a stem. This type of neuron does not have dendrites. (C) A receptor neuron, in this case a photoreceptor from the retina, that has neither an axon nor dendrites.

can vary greatly among cell types from a few micrometers to a meter or more. Most axons remain within the central nervous system, but some leave the central nervous system and end on muscles or glands; these axons are called effectors or motor neurons. The neuron illustrated in Figure 2-1(A) is typical of motor neurons that control muscles of the skeleton. Its axon would leave the central nervous system and travel to a muscle where it would divide into a series of branches before terminating on the muscle fibers.

Not all neuron somata (plural of soma) have dendrites. Figure 2-1(B) illustrates a neuron type that has no dendrites in the conventional sense. Its principal source of stimulation is not another neuron at all but rather is some event outside of the central nervous system. It is a sensory receptor neuron, and, like the effector neuron in Figure 2-1(A), it too has most of its process in the environment outside of the central nervous system. In this case, however, the process is actually a very long dendrite. At the right are its receptor branches, which might be under the surface of the skin or wrapped around a small group of muscle fibers to detect muscle stretch. Other such sensory branches might be in contact with specialized receptor cells, such as those that detect light or electric fields, or one of the different types of hair cells that detect the movement of fluids in the auditory or vestibular systems. Mechanical deformation of the receptor branches or activation of the specialized receptor cell activates this sensory or receptor neuron to send a signal along its process and past its cell body, after which point the process is a true axonal fiber, and then to the axon terminals that end on neurons within the central nervous system. Other receptor types detect chemical changes in the external and internal environments.

The soma of this type of neuron typically remains outside of the central nervous system in a sensory **ganglion** and does not participate directly in the process of conduction of the propagated signal. It provides nutritional and metabolic support to the dendritic and axonal parts of its process but is not an active player in the flow of information into the central nervous system. Some sensory neurons, however, have their somata within the central nervous system.

Figure 2-1(C) represents a type of sensory neuron, a photoreceptor, that is specialized for the detection of photons of light. These are the receptors of the eye that convert the energy of light into signals that can be conducted to the brain. The photoreceptor end is activated by photons of light and in some sense can be thought of as a highly specialized dendrite. Activation of the photoreceptor eventually leads to the development of a signal that is conducted along the cell to a terminal where it contacts another neuron that conducts the signal further into the central nervous system.

TRANSPORT WITHIN NEURONS

The soma produces many materials that are important for the maintenance of the internal and external workings of the neuron. These materials include enzymes and other substances that participate in the synthesis of neurotransmitters and neuromodulators; proteins for use in the formation of synaptic vesicles, ion channels, and membrane receptors; and proteins for the maintenance of the neuron's internal skeleton. Still other materials are necessary for maintenance of the cell membrane,

which is the boundary between the inside and outside of the cell. Finally, used synaptic vesicles, depleted mitochondria, and other organelles must be returned to the soma for reuse or for digestion in the lysosomes and subsequent "recycling" into new membrane.

The often extreme separation between the soma and the axon terminals and between the soma and the tips of the dendritic branches is too great for simple diffusion to function effectively. Neurons therefore have a kind of intraneuronal circulatory system to move secretion products from the soma to the remote ends of the neuron. There are, in fact, three separate transport systems within the neuron: a fast anterograde (forward moving) transport system that carries materials from the soma towards the axon terminals and dendritic branches, a fast retrograde (backwards moving) transport system in the reverse direction, and a slow axoplasmic transport system.

The fast anterograde transport system, which can move as fast as a meter a day, makes use of one of the neuron's internal skeletal elements, the microtubules, which are slender tubes that run the length of the axon. Rather than flowing through these tubules, which have too narrow a diameter in any case, the organelles are transported along the surface of the tubules by a "motor molecule" called kinesin. The fast retrograde transport, which is involved in the return of used materials to the soma for recycling, moves at a slower speed than the anterograde fast transport. The returning materials are packaged in membranes and are transported along microtubules in a manner similar to that of the fast anterograde system except that a different motor molecule, in this case dynein, moves the membrane packages along the microtubules.

The slowest (1–10 mm/day or slower) of the three transport systems is the slow axoplasmic transport system, which consists of two components: a slow system and a very slow system. The slow system carries proteins that, among other things, coat the synaptic vesicles. The very slow system carries the proteins that maintain the filamentous internal skeleton of the neuron: the microtubules, neurofilaments, and microfilaments. The ability to chemically mark many of the substances being transported within neurons has served as one of the most powerful means of visualizing the connections between neuronal populations. The similarities and differences in the patterns of connections are among the major criteria for determining evolutionary trends within the nervous system.

CLASSIFICATION OF NEURONS

Somata

Neurons may be classified in a variety of ways. Figure 2-2 shows one type of classification. The figure shows a monopolar cell without dendrites on the soma. The bipolar cell has fine dendritic branches at the left and its axon at the right. Such cells are found in the retina of the eye. The multipolar cell is the most common type found in the vertebrate central nervous system; it is shown in Figure 2-2 with many thick dendrites and finer dendritic branches on the left and an axon on the right.

Dendrites

Another system of neuronal classification is presented in Figure 2-3, which shows neurons with several different types

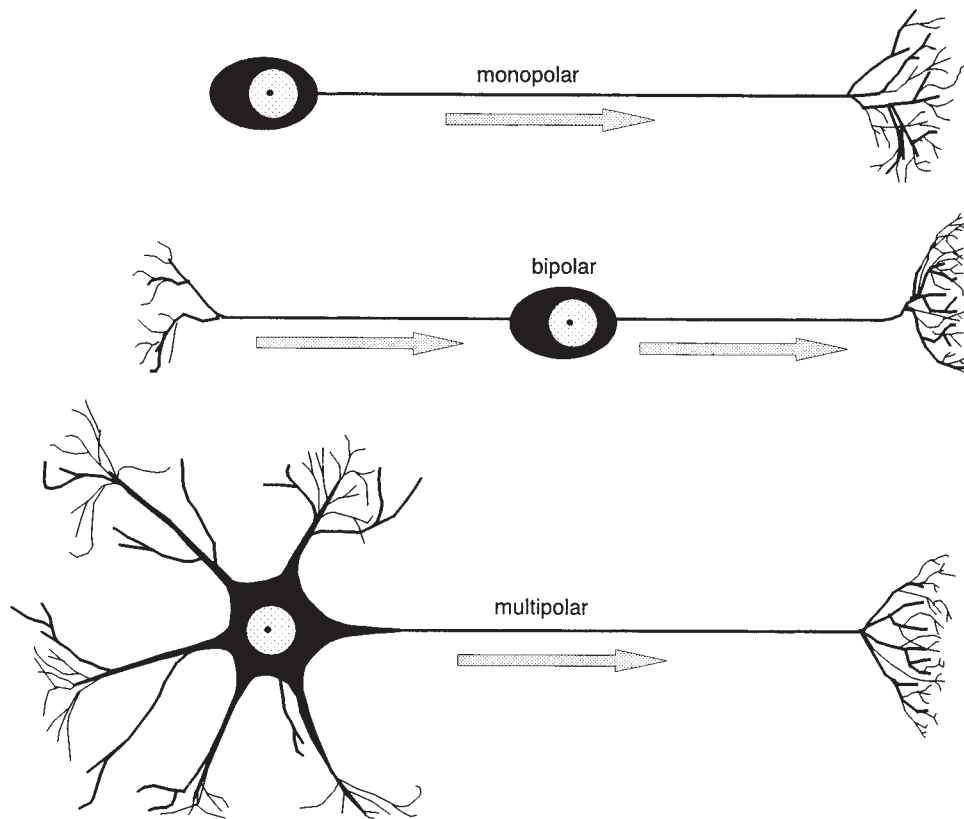


FIGURE 2-2. Three types of neurons classified according to the number of poles. The arrows indicate the direction of conduction of the nerve impulse.

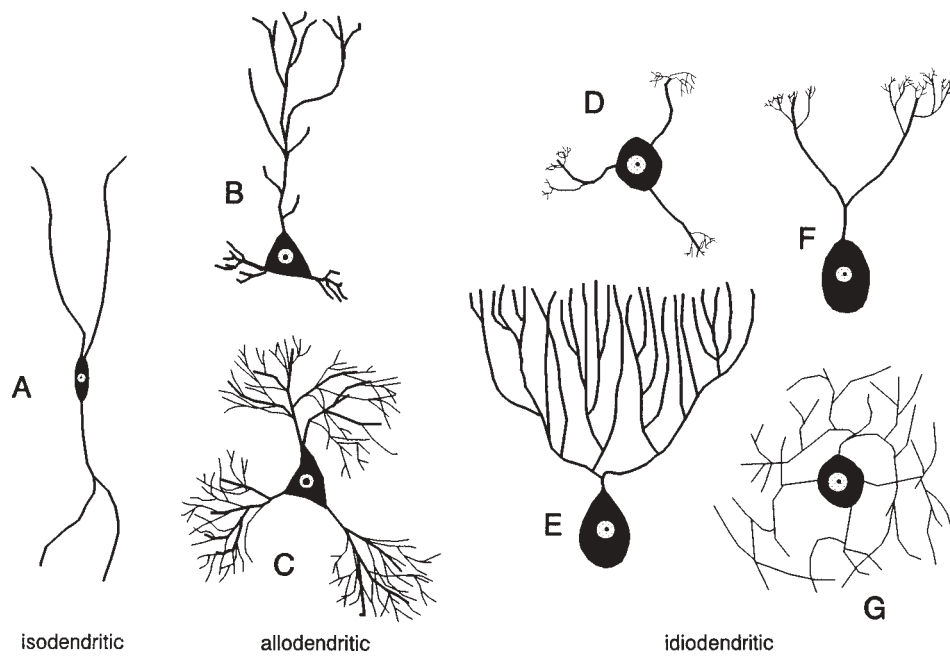


FIGURE 2-3. A classification of neurons according to the type of dendritic tree. Their axons are not shown.

of dendrites. The classification of dendritic types is based on the work of Enrique Ramon-Moliner. The dendrites of the neurons in Figure 2-3(A) are long and slender without many branches and are called **isodendrites**. The neurons in Figure 2-3 (B and C) have branched dendrites and can achieve fairly high degrees of complexity and specialization. These are known as **allodendrites**. The most specialized are called **idio-dendrites**, which are represented in Figure 2-3 (D–G), typically are found in regions of the nervous system such as the olfactory bulb or cerebellar cortex.

Figure 2-4 depicts two neurons with their dendrites and a portion of their axons. The cell on the left is known as a pyramidal cell because its soma has the shape of a pyramid; the other is called a piriform cell because its soma is roughly in the form of a pear. In each case, two sets of dendrites are shown: a long dendrite ascending from the peak or apex of the cell (hence called “apical” dendrites) and other dendrites protruding from the base of the cell (the “basal” dendrites). Each of these dendrites subdivides into dendritic branches that increase the dendritic surface area.

Dendrites offer an enormous surface area for axon terminals to end upon. This huge surface provides termination sites for thousands of axon terminals. Some of these terminals are excitatory and contribute to depolarizing the dendrite and soma; others are inhibitory and thus contribute to hyperpolarizing them. Rarely does a single axon terminal have sufficient influence to excite a neuron to produce an action potential or to inhibit it. Summation of the activity of many synapses therefore usually is required in order to influence a neuron’s actions. Often the generation or suppression of an action potential is the result of a kind of algebraic summation of the excitatory and inhibitory influences on the cell. If the sum of the excitatory influences outweighs the sum of the inhibitory influences, and if the net excitatory influences are present in sufficient quantity, the action potential or nerve impulse will be generated in the axon hillock and conducted down the axon. Den-

drites thus are a battleground on which the opposing forces of excitation and inhibition compete. Because of their varying thicknesses and varying distances from the axon hillock, dendrites serve not merely as the input end of the neuron, but as integrators of neuronal activity. They provide areas in which weak incoming signals can combine to form stronger influences on the ultimate action of the cell.

Axons

Neurons also may be classified according to their axons. At one extreme are the many small neurons that have no axons at all. These axonless neurons are involved only in local neuronal activity that is confined to a circumscribed cell population; since they do not exert an influence on distant cells, they need no axons. At the other extreme are neurons with exceptionally long axons, such as those that travel from the spinal cord down the length of the hind leg of a tetrapod and move its toes. Axons also vary in thickness, from the giant axon of the Mauthner cell to the tiny axons of the olfactory nerve. The effective thickness of an axon depends in part on the diameter of the axon itself, and in part on the diameter of its myelin sheath. The total diameter of the axon (axon plus sheath) is a major determiner of the velocity of conduction of the action potential. In general, larger diameter axons conduct more rapidly, although other factors play a role as well.

SYNAPSES

Chemical Synapses

The surface of the axon terminal where it contacts the neuron is known as the presynaptic membrane; the specialized surface of the neuron that receives the axon terminal is known as the postsynaptic membrane, below which is a specialized region of the dendrite’s cytoplasm. The synapse itself is a small extracellular space that is about 20–30 nm across (1 nm is 1/1,000 of a μm). Within the axon terminal are small, membrane-bound packets or “vesicles,” which contain chemical substances that are released into the synaptic space by the arrival of the action potential. These chemicals excite or inhibit the postsynaptic membrane and are one of the ways that one neuron can affect the activity of another neuron. Also contained within the axon terminal are one or more mitochondria. The mitochondria are sources of energy for biological processes and are found in the soma, the synaptic vesicles, and wherever the neuron is highly active. Because the transmission of a signal across the synapse in this case is chemical, this synapse is known as a chemical synapse.

The events that occur in a chemical synapse are shown in Figure 2-5. Figure 2-5(A) shows a synaptic terminal at rest. The axon terminal filled with synaptic vesicles is shown just above the synaptic space. The terminal membrane that faces into the space is the presynaptic membrane. Below the synaptic space is the postsynaptic membrane with protein receptor sites. When the action potential arrives at the terminal, it causes calcium channels to open, which allows an influx of calcium ions. The arrival of the calcium influx in turn results in a forward movement of the vesicles with their contents of neu-

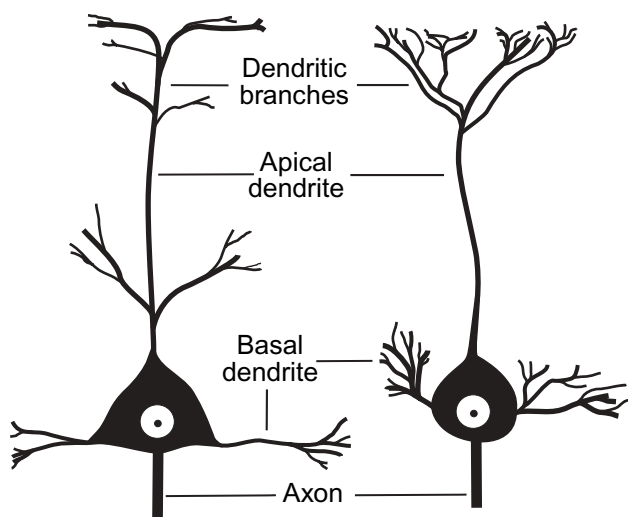


FIGURE 2-4. Examples of dendrites in neurons with different shaped somata. The initial segment of each cell’s axon is shown at the bottom.

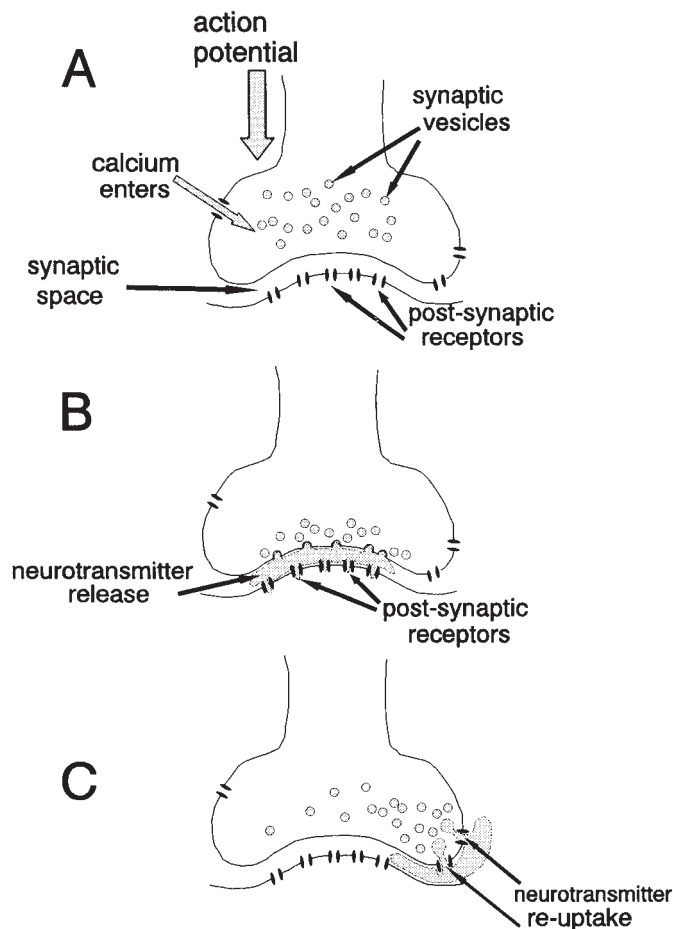


FIGURE 2-5. Transmission in a chemical synapse. (A) Neuroactive chemicals are stored in synaptic vesicles. Calcium enters through a calcium channel. (B) The vesicles move toward the synaptic membrane and fuse with it, thereby releasing their chemical contents into the synaptic space where they are taken up by receptors in the postsynaptic membrane. (C) Reuptake of excess neurotransmitter material from the synaptic space and its reincorporation into vesicles for future use.

rotransmitter substances towards the presynaptic membrane. As shown in Figure 2-5(B), the membranes of the vesicles fuse with the neuronal membrane, allowing the contents of the vesicle to be released into the synaptic space where they can act upon protein receptors in the postsynaptic membrane. If the transmitter substance is excitatory (i.e., depolarizing), it generates an excitatory postsynaptic potential in the postsynaptic membrane. If the substance is inhibitory, its action on the postsynaptic membrane is as if it had increased the polarization of the cell; that is, increased the resting potential thereby making it more difficult to generate an action potential, a phenomenon called hyperpolarization. Figure 2-5(C) shows that excess neurotransmitter material that remains in the synaptic space may be taken back into the terminal by other channels to be reincorporated into vesicles for future use.

Neuroactive Substances

Chemical synapses may be characterized by the chemical compounds present in them. Apart from their functions in

synaptic transmission, these compounds are useful to comparative neuroanatomists because they can serve as markers of neuronal pathways and populations in different taxonomic groups. Thus they become another indicator of brain evolution and adaptation to the environment. Table 2-1 lists some of the major neuroactive compounds. These fall into a variety of categories. The two major categories are neurotransmitters and **neuromodulators**. Within each of these categories are several groups of chemicals. The neurotransmitter category contains relatively few compounds; the neuromodulator category has more than 30 compounds, only some of which are listed in the table. The cholinergic neurotransmitter is acetylcholine, which is excitatory or inhibitory. The biogenic-amine neurotransmitters, epinephrine (adrenalin), norepinephrine (noradrenalin), dopamine, serotonin, and histamine may likewise have excitatory or inhibitory actions depending on the type of receptor they encounter. The amino acid neurotransmitters consist of two usually excitatory transmitters, glutamate and aspartate, and two usually inhibitory transmitters, γ -aminobutyric acid (GABA) and glycine.

TABLE 2-1. Some of the Major Neuroactive Substances in the Central Nervous System

Type	Chemical Group	Substance	Function
Neurotransmitters	Cholinergic	Acetylcholine	Excitatory or inhibitory, depending on the type of receptor
	Biogenic amines	Norepinephrine	
		Epinephrine	
		Dopamine	
		Serotonin	
		Histamine	
	Amino acids	Glutamate	Excitatory (usually)
		Aspartate	Inhibitory (usually)
		GABA ^a	
		Glycine	
Neuromodulators	Peptides and hormones	VIP ^b	Modulation of synaptic transmission by affecting transmitter release or reuptake or by changing the sensitivity of the postsynaptic membrane for the transmitter
		Substance P	
		Methionine-enkephalin	
		Leucine-enkephalin	
		Cholecystokinin	
		Somatostatin	
		Neurotensin	
		Bombesin	
		β-Endorphin	
		Angiotensin II	
		Glucagon	
		Bradykinin	
		Calcitonin	
		Neuropeptide Y	
		Anterior pituitary hormones ^c	
		Posterior pituitary hormones ^d	
		Hypothalamic hormones ^e	
		Insulin	
	Second messengers	Cyclic AMP	
		Arachidonic acid	
		Diacycloglycerol	
		Cyclic GMP	

^a γ-Aminobutyric acid.^b Vasoactive intestinal polypeptide.^c These include: adrenocorticotrophic hormone (ACTH), prolactin, luteinizing hormone, growth hormone, and thyrotrophic hormone.^d Oxytocin and vasopressin.^e These include: thyrotrophic hormone releasing hormone (TRH), gonadotrophic hormone releasing hormone (GnRH), corticotrophic hormone releasing hormone (CHRH), and growth hormone releasing hormone (GHRH).

The neuromodulators generally do not directly affect the depolarization or hyperpolarization of neurons as do neurotransmitters (although some have been reported to have these properties). Instead, the neuromodulators influence the duration or intensity of the action of the neurotransmitters by affecting the reuptake of transmitters, the effectiveness of the enzymes present in the synapse, the rate of transmitter release, and a variety of other phenomena, which make the synapse very different from a simple on-off switch. A vast array of pos-

sibilities for subtle and sophisticated modifications of the transfer of information between neurons is made possible by these many substances.

In addition to modulating synaptic transmission, many of these versatile chemical compounds play other roles in the body; indeed many of their names may be familiar to you in other contexts. Some of these peptides are gastrointestinal peptides such as vasoactive intestinal polypeptide (VIP), substance P, cholecystokinin, and neurotensin. Others are hormones that

are secreted by the posterior division of the pituitary (oxytocin and vasopressin) and are involved in the regulation of blood pressure and affect maternal functions and various aspects of social behavior. Others are releasing hormones that are secreted by the hypothalamus, such as thyrotropin releasing hormone (TRH), luteinizing hormone releasing hormone (LHRH), and growth hormone releasing hormone (GHRH). Still others are anterior pituitary hormones, such as adrenocorticotrophic hormone (ACTH), growth hormone, and luteinizing hormone. Yet others are naturally occurring opioids, such as methionine-enkephalin, leucine-enkephalin, and β -endorphin. Finally, some second messenger substances, such as cyclic AMP, arachidonic acid, diacylglycerol, and cyclic GMP, which functions in retinal photoreceptors, also have neuromodulator properties.

Electrical Synapses

Not all synaptic junctions make use of chemical substances as the transmitter or modulator. At many synaptic junctions, the transmission is carried out by the passage of electrical current across the synapse. These are known as “electrotonic” or “electrical” junctions or simply “gap” junctions. The synaptic space of an electrotonic junction is only 2–4 nm across, which is only about one-tenth the width of a chemical synapse. Present on each side of the gap are matching pores or ion channels that can be opened and closed by means of a complex of proteins. When these proteins twist, the pore is opened, which allows the ionic current to flow across the gap. Electrical junctions provide for synaptic transmission with virtually no delay because no time is lost as vesicles move to the presynaptic membrane and discharge their chemical transmitters. Electrical junctions also are not subject to “fatigue” as are chemical junctions, which can deplete their supply of vesicles if stimulated too frequently. Most electrical junctions can transmit their electrical signals in either direction, whereas chemical junctions can only transmit from the presynaptic to the postsynaptic membrane. Finally, transmission at electrical synapses is much faster than at chemical synapses.

Electrical synapses are found mostly in invertebrate nervous systems. In spite of their several advantages, they tend to be rather stereotyped in their action and do not lend themselves well to the subtle and varied types of interactions and modulations that are possible in a chemical transmission system. Indeed, the huge variety of possible types of interactions that can occur in a chemical system is a major contributor to the vast array of complexity of behavior that is characteristic of vertebrates and that has played such an important role in their evolution.

Volume Transmission

Many instances of intercellular communication in the nervous system occur via chemical synapses, with the neurotransmitter or neuromodulator release occurring in the immediate vicinity of a postsynaptic dendritic site, or via electrical synapses; however, a different kind of neuronal cell communication, called **volume transmission**, also occurs. Volume transmission, also referred to as nonsynaptic transmission, parasympaptic transmission, or paracrine transmission, was iden-

tified and described by Miles Herkenham in 1987, and the reader is referred to his paper as well as to the comprehensive review of this subject by Rudolf Nieuwenhuys, published in 2000, for in depth treatments of this often overlooked phenomenon.

Volume transmission involves the release of neuroactive substances at presynaptic sites that are not positioned close to any postsynaptic sites, thus necessitating diffusion of the released neurochemical to relatively distantly located sites for their activity to be realized. It is common across invertebrates as well as in vertebrates. In the latter, it particularly characterizes the systems that run within the most central portion of the brain and that are involved in emotional and/or visceral types of functions. Nieuwenhuys characterized this central, or medial, part of the brain as a “greater limbic system,” referring to various regions of the brain, from the spinal cord through its most rostral levels, that are involved in emotions, learning, memory, and a number of related processes (see Chapter 30) and noted that volume transmission is a particular feature of it. According to this scheme, this medial part of the brain contrasts with the more lateral part, in which the pathways are characterized by chemical synaptic transmission and involved in the more “objective” relay and analysis of incoming sensory information and outgoing motor commands.

NEURONAL POPULATIONS

Anatomists frequently refer to a discrete population (or to two or more populations) of neurons, often situated within a well-circumscribed boundary, as a **nucleus**. The same term is also used to refer to the intracellular structure that contains the DNA of the cell. Fortunately, the potential for confusing these two uses of the term is minimal because the contexts are so different. Examples of such “population nuclei” are the dorsal division of the lateral geniculate nucleus of the visual system, the nucleus ovoidalis of the avian auditory system, and the motor nucleus of the trigeminal nerve, which are structures that will be described in detail in later chapters. In the brain, alternate terms for nuclei include locus (e.g., locus coeruleus), substantia (e.g., substantia nigra), area (e.g., area postrema), and ganglia (e.g., basal ganglia).

One of the hallmarks of nuclei is that the dendrites of the neurons remain within the boundary of the nucleus. A nucleus may consist of several layers, or laminae; however, the dendrites of neurons within each lamina remain within it and do not extend beyond the laminar boundary into the territory of another lamina. In contrast, the term **cortex** is used to denote multiple populations of neurons that are arranged in layers; in most layers, the dendrites of neurons extend across the territory of multiple other layers. The following sections address nuclei, but most of the material in them applies to cortices as well.

Golgi Type I and II Cells

Population nuclei often consist of more than one type of neuron. The nineteenth century Italian anatomist, Camillo Golgi, distinguished two types of cells within the boundary of a nucleus. The **Golgi Type I neuron** tends to have a large soma

and a long, thick, well-myelinated axon. This axon passes outside of the confines of the nucleus and can travel considerable distances; those that pass from nuclei of the brain into the spinal cord of a large animal, such as a giraffe or a whale, can be more than a meter in length. Often the axons of Golgi Type I cells have side branches, called **collaterals**, that permit the axon to contact other nuclear populations en route to its final destination. The various Golgi I axons from the same nucleus typically travel together in bundles (often known as “tracts” or “fiber bundles”) as they make their journey to their target neurons.

In contrast, the **Golgi Type II neuron** has a small cell body and short, often unmyelinated axons. These axons rarely pass outside the boundary limits of the nucleus. Some Golgi Type II neurons have no axons at all. Thus their dendrites both receive input from other neurons (axo-dendritic terminations) and make synaptic contact with the dendrites of other neurons (dendro-dendritic contacts). Similar points of contact can be found with the soma. The Golgi Type II neurons are critical for the functioning of the individual population components of the nervous system. They form local circuits within the nucleus that contribute to whatever the function of the particular nucleus might be, such as the processing of information or the patterning of rhythmic events. Golgi Type II neurons are often referred to as **local circuit neurons** or **interneurons**. Figure 2-6 shows Golgi Type I and Golgi Type II neurons.

To understand the differences between the Golgi I and II cells, consider that the Golgi II cells are like a local telephone network that maintains communication within a factory and allows the workers to perform their tasks in an integrated and coordinated manner. The Golgi I cells are like a long-distance telephone network that permits factories that are located at considerable distances from one another to be in contact and to coordinate their activities.

Nuclei and Planes of Section

In order to study the anatomy of the central nervous system, anatomists often cut the neural tissue into very thin

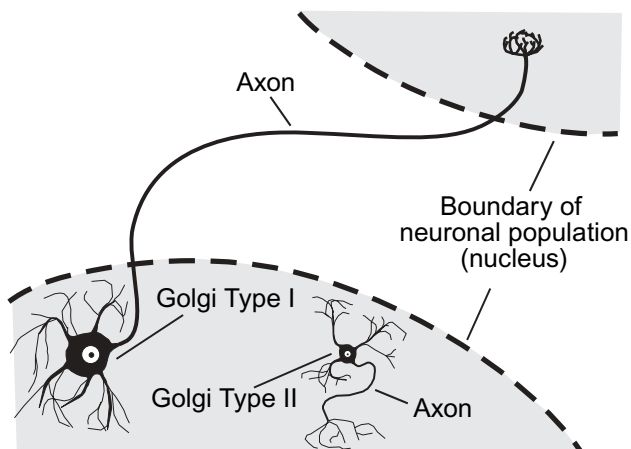


FIGURE 2-6. A Golgi Type II neuron, the axon of which remains within its neuronal population, and a Golgi Type I neuron, which sends its axon to a different neuronal population.

slices called “sections” (5–50 μm or thinner), so that they may be examined under a microscope. These sections pass through nuclei and through the axonal bundles or tracts that pass from one nucleus to another. While these sections give an accurate view of the cross-sectional extent of a nucleus or axon bundle, they give no indication of how much of these structures may extend ahead of or behind the plane of the section. Many of the illustrations in this book consist of sections through the brain or spinal cord, and the reader should understand that the ovals, ellipses, circles, and other shapes that appear in the section only represent a single slice through what may be a much larger and much more complex structure. This is diagrammed schematically in Figure 2-7. At the left, represented by the thicker cylinder, is a nucleus with its large Golgi Type I neurons and smaller Golgi Type II neurons. The Golgi Type I axons leave the nucleus and enter an axon bundle, represented by the smaller cylinder. The gray rectangle represents a section through these two structures. To the right of the arrow is the section showing how the nucleus and axon bundle would appear in this single plane. The Appendix describes in detail the planes of section conventionally used in neuroanatomical studies.

Techniques for Tracing Connections Between Nuclei

The second half of the twentieth century was a period of unprecedented new knowledge about connections between neuronal populations in the central nervous system. This explosion of information was largely due to the development of a vast number of new techniques based on a variety of biological principles. Prior to this period, neuroanatomists could only

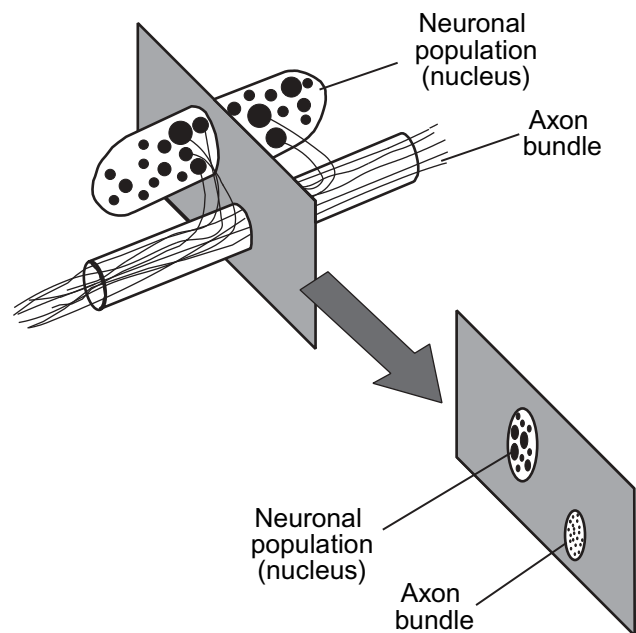


FIGURE 2-7. The appearance of a neuronal population and a nearby axon bundle in a three-dimensional view and in a transverse section through both.

rely on methods that stained neurons in an unpredictable manner. To target a specific population of neurons for study, they could only use methods that were based on the degenerative processes that follow injury of the cell soma or separation of the axon from the soma.

Since the second half of the 19th century, anatomists had been able to visualize neurons or parts of neurons using aniline dyes or metallic deposits. The Golgi technique, in which silver impregnation was used to visualize whole neuronal cell bodies and the full array of their dendritic processes, is an example of one of the metallic impregnation methods. This method is still in use today. Its main drawback as a tracing method is the fact that the one cannot predict ahead of time which neurons will be impregnated by the silver.

The problem was how to target a specific group of axons for study and then to identify them from among the vast number present in the microscopic image as the anatomist went from one section of brain tissue to the next. One of the first tracing methods consisted of injuring the neurons to be studied and then using the resulting degenerative process as a tag or label to trace the course of their axons. Degenerative changes in the soma separated from all or part of its axon (retrograde degeneration) could be observed with the traditional aniline dyes that had been used during the 19th century. The deposited metal could then be reduced so that it appeared black and thus visible under the microscope. The location of the degenerating axoplasm and the terminal endings of the axons could then be traced and charted in serial sections, and the axonal pathway from one point to another within the nervous system could be reconstructed. Degeneration of the separated axon (anterograde degeneration) could be studied by impregnating the degenerated axoplasm with silver or the degenerated myelin with osmium.

The initial phase of the technical revolution of the 1960s and 1970s depended on newer methods of silver impregnation that were developed at that time (the Nauta-Gygax stain and its variants, and the Fink-Heimer stain); these methods allowed for much more precise tracing of connections by suppressing the appearance of silver in normal axons, which made the degenerating axons easier to see, and later by permitting visualization of the actual axon terminals rather than just the axons. These 20th century silver methods also were more effective in both mammalian and nonmammalian vertebrates than previous techniques; they opened the way for a greater exploration of connections in nonmammals than could previously have been attempted.

The techniques currently in use do not require lesions of nervous tissue but instead involve injecting one of a number of tracer substances into a particular site and allowing the intracellular transport processes (axonal transport or axoplasmic flow) to distribute the substance along the length of the axon to its terminals and its cell soma. Histological procedures are then carried out on serially sectioned material, as in the reduced silver methods, and the location of the labeled axons, axon terminals, and cell somas are charted under the microscope. A number of the labeling substances can be visualized at both the light and electron microscopic level. The tracing substances that are most commonly used include tritiated amino acids, horseradish peroxidase (HRP), HRP conjugated to

wheat germ agglutinin (WGA), and the plant lectin *Phaseolus vulgaris*-leukoagglutinin (PHA-L).

The large repertoire of axonal transport tracing techniques that has been developed has greatly enhanced our ability to visualize and trace connections. The tracing substances currently available vary widely in how they can be visualized. For example, some can be visualized by histological procedures in which the substance is reacted in various solutions to acquire a color or be tagged with a colored substance that is visible under the microscope. Other tracing substances fluoresce when illuminated with ultraviolet (UV) light. Still other tracing substances are radioactive and can be visualized by applying a thin layer of photographic emulsion over the sections, exposing the emulsion for a certain period of time, and then developing the emulsion just as one would develop a photographic print. The pattern of radioactive emissions then can be charted in serial sections to reveal the course and terminal site of the axonal pathway being studied.

This wide variety of tracing substances and visualization techniques has permitted much sophisticated and elegant experimental work. Double and even triple labeling of different components of a neuronal circuit has been developed to a fine art. For example, one might label one set of afferent axons of a nucleus with one fluorescing tracer, a second set of afferent axons with a different fluorescing tracer that fluoresces under a different wave-length, and the neuronal cell bodies and their dendrites in the nucleus with a retrogradely transported tracer that can be visualized with histological processing. The precise synaptic pattern of the two different sets of afferent fibers on the postsynaptic neurons within the nucleus can thus be worked out.

A number of additional tracing techniques exist that do not depend on axonal transport mechanisms. Some take advantage of the natural fluorescence of some of the neuronal transmitters, such as serotonin and dopamine. Widespread use is also currently made of immunohistochemical methods for antibody labeling of neuroactive substances, such as some of those listed in Table 2-1, which then can be visualized with histological techniques. In addition to axonal tracing methods, techniques allowing *in vivo* and *in vitro* study of particular parts of the brain, whole-brain scanning techniques, extra- and intracellular electrophysiological recording techniques, *in situ* hybridization techniques for localizing sites of gene expression, and an extensive array of additional such methods allow for a truly comprehensive approach to the study of the organization and function of the central nervous system.

Table 2-2 gives some examples of the more commonly used contemporary methods as well as some of the earlier methods. The table is not intended to be an exhaustive survey but rather gives a sample of the many different methods that you are likely to encounter if you read any of the works listed at the ends of chapters in this book or elsewhere in the neuroanatomy literature.

RECEPTORS AND SENSES

The senses are our windows onto the world—both the world outside and the world within our bodies. We cannot know anything about either of these worlds except through our

TABLE 2-2. Summary of Methods for Tracing Connections in the Central Nervous System

Method Type	Examples	Comments
Retrograde degeneration	Nissl stain	Aniline dye stain of a soma separated from part or all of its axon
Anterograde degeneration	Marchi stain	Impregnation with osmium of degenerating myelin of an axon separated from its soma
Reduced silver	Golgi stain Cajal stain Bielschowsky stain	Impregnation of neurons with reduced silver
	Nauta-Gygax stain	Especially effective on axons that are degenerating due to separation from their somata
	Fink-Heimer stain, de Olmos stain	Especially effective on degenerating axon terminals
Anterograde and/or retrograde axonal transport and/or diffusion along axonal sheaths	Autoradiography	Transported along axons and visualized with photographic emulsion, fluorescence, chromagen (attachment of chemical dye that can be reduced and visualized), or other histological techniques
	<i>Phaseolus vulgaris</i> -leucoagglutinin (PHA-L)	
	Horseradish peroxidase (HRP)	
	Fluorescent dyes (Evans blue, fast blue, fluorogold, Di-I, Di-O)	
	Rhodamine beads Cholera and other toxins	
	Wheat germ agglutinin-horseradish peroxidase (WGA-HRP), tritiated proline	
Immunohistochemistry	Various neurotransmitters and neuropeptides, mRNA, and related compounds	Antibodies used for visualization with fluorescence or other microscopy methods

sensory systems. Of course we can know a lot about both worlds with the use of scientific instruments, but even this information must come to us via the sensory systems. The senses are our way of detecting energy or chemical substances in the inner and outer worlds. The detectors for the external world are known as **exteroceptors** and those of the inner world are known as **interoceptors**. Exteroceptors are the receptors for vision, taste, smell, touch, warmth, cold, and so on. Interoceptors provide the central nervous system with information about events within the body, such as the distension of the gastrointestinal system and urinary bladder, pressure of the blood in certain blood vessels, and levels of various substances in the blood such as glucose, fat, and various hormones.

The types of energy detected are:

- The electromagnetic spectrum, which includes visible light (i.e., light visible to humans), ultraviolet and infrared portions of the spectrum, and electricity and magnetism.
- Mechanical energy, such as is produced by bending, stretching, shearing, and compressing of the skin or other tissues.
- Chemical energy, which is the energy released by the reactions of chemical substances in the environment with the chemicals that make up the receptor.

How Many Senses?

How many senses are there? When this question is asked, we usually think of five: taste, touch, smell, hearing, and vision. Sometimes we refer to an elusive “sixth sense,” by which we really mean “intuition,” which is not an energy detector at all. However, there are many more than the proverbial five or even six senses. When we take into account the full range of senses available to vertebrates, we can count something in the neighborhood of 20 senses, depending on how fine one wishes to subdivide the different receptor types. These include the traditional five, plus pain, vestibular sense, temperature, the various types of touch (deep, light, vibration), proprioception (the positions of joints), muscle stretch, etc., the ability to detect electrical fields (lampreys, sharks, some ray-finned fishes, some amphibians, and monotremes), infrared radiation in a manner similar to vision (some snakes), lateral-line sensations (nontetrapods, amphibian larvae, and some adult amphibians), and magnetic fields (some fishes, amphibians, and birds).

Receptors and Awareness

Events that occur in the internal or external worlds that do not affect our interoceptors or exteroceptors are unknown

to us. For example, many animals can detect light in the ultraviolet portion of the spectrum. No doubt they see it as some sort of color. Because we are unable to detect light energy in this portion of the spectrum, as far as our personal experience is concerned, this part of the spectrum does not exist. We can only know of its existence with the aid of specialized scientific instruments. Similarly, many mammals, including bats, many rodents, and dogs, can hear sounds that are much too highly pitched for us to hear. Even within our own bodies, receptors are at work, participating in the precise regulation of bodily functions such as blood pressure, the flow of materials through the digestive system, the secretion of hormones, all without any awareness on our part because the information from these interoceptors never reaches those brain regions that bring such information to our conscious awareness. For example, a complex series of neural circuits produces a precise regulation of the diameter of the pupil of the eye according to the intensity of light present in the external environment. We are totally unaware of these adjustments, which are being made each time the light level changes. We can become aware of some of our senses if we produce certain types of disturbances of their mechanisms. For example, we are normally unaware of the operation of the vestibular organs in the middle ear, which provide us with information about the pull of gravity, the acceleration of our bodies, the position of our head, and so on, so that the necessary postural adjustments can be made to keep us in our erect posture and prevent us from falling over as we change position or try to walk on an uneven surface. These adjustments are, for the most part, totally transparent to us. If we spin ourselves round and round, however, as most of us did as children, we quickly become aware of a variety of sensations that result from the abnormal stimulation of this sensory system.

Sensory Experience as a Private Mental Event

To return to the detection of ultraviolet light, a feat that we are incapable of, we suggested that those animals that can detect ultraviolet light probably experience it as some sort of color. What color is ultraviolet? We cannot imagine what ultraviolet color looks like any better than we could describe the colors of a sunset or autumn leaves to a person who has been born blind. Sensations are private mental events knowable only to the person or animal having the sensory experience. Indeed, you have no way of knowing for sure that what you experience as red when looking at an apple is what a bird or another mammal experiences when it sees the same apple. This may sound a bit philosophical, but it is of relevance to the fact that we cannot know, nor can scarcely imagine, what the subjective experiences are of animals that have senses very different from our own. For example, birds have more photopigments, which makes them more sensitive to certain regions of the light spectrum than humans, and therefore they almost certainly do not see objects as having the same colors as we do. What does a snake experience when it uses its infrared-detecting pit organs to detect a mouse in total darkness? Possibly it is something akin to vision, but we cannot know what it is like for the snake. Likewise, what does electroreception feel like to an animal that can detect minute changes in the electrical fields present in the surrounding environment? What is it like to have

taste receptors all over one's body as do certain fishes? Some birds appear to have the capability to navigate by means of the earth's magnetic fields. What does a magnetic field feel like to them? There is no way for us to know the answers to any of these questions.

Sensory Adaptation

A property of receptors is that they decrease their responsiveness to persistent stimuli. This phenomenon is referred to as **adaptation**. Adaptation is not a voluntary act like a human or an animal shifting its attention to and from specific stimuli at will; rather, it is more like a receptor fatigue phenomenon and only can be reversed by a period of absence of the stimulus or by changing the stimulus. You most likely have experienced adaptation of the olfactory system when you entered a room with a particularly strong odor, but after a few minutes in the room, you no longer notice the odor, even if you try. Some receptors become adapted to a particular level of stimulation and will only respond to a different level. This property sometimes results in strange effects. If you put one hand in very cold water and the other hand in very warm water, leave them for a few minutes, and then put both hands in water that is at room temperature, you will observe that the hand that was in the warm water feels cold and the hand that was in the cold water feels warm, yet both are receiving the same stimulus of room temperature water.

RECEPTOR TYPES

Table 2-3 presents a classification of receptors according to their functional classes, sensory modalities, and receptor types. All of these receptors are neurons or neuron-like cells. As is the case with all neurons, a resting potential is maintained across the cell membrane. When activated by the appropriate energy, the ionic events that maintain the resting potential are disturbed and a receptor potential results. The process by which mechanical, chemical, or electromagnetic energy is converted to neural events (i.e., the electrochemical process that produces receptor potentials) is known as **sensory transduction**.

Receptor potentials are produced by the receptor cells in response to stimulation by the appropriate stimulus. They are like the local potentials of neurons in that they are graded potentials; that is, the magnitude of the potential is proportional to the intensity of the stimulus that is being applied to it. If the receptor potential achieves a sufficient magnitude, an action potential develops in the axon of the sensory neuron. This action potential sweeps down the axon to the terminals located in the brain or spinal cord. These terminals release their neuroactive chemical and the process of sensation has begun.

Some receptor cells are true sensory neurons with either free sensory terminal endings or with specialized sensory terminals. Like other types of neurons, receptor cells with specialized endings have an axon that terminates within the central nervous system. This type of receptor cell is typical of the skin, muscle and joint senses, of touch, pain, stretch, and so on. Some examples of these types of receptors are shown

TABLE 2-3. A Classification of Receptors and Their Senses

Receptor Class	Sensory Modality		Receptor Type
Mechanoreceptor	Touch	Fast adapting	Meissner's corpuscles
		Slow adapting	Merkel's disks
	Tendon stretch		Tendon organs
	Skin stretch		Ruffini endings
	Joint position		Joint receptors
	Muscle length and stretch		Muscle spindles
	Muscle contraction		Golgi tendon organ
	Vibration		Pacinian corpuscles
	Hearing		Hair cells
	Vestibular (gravity, acceleration, head position)		Hair cells
	Lateral line		Hair cells
Radiant-energy receptor	Light (including UV)		Photoreceptors
	Infrared radiation (pit organ)		Pit-organ receptors
	Infrared radiation (skin warmth)		Free nerve endings
	Infrared radiation (skin cold)		Free nerve endings
Chemoreceptor	Taste		Taste buds
	Smell		Olfactory receptors
Electroreceptor	Electric fields		Ampullae
			Tuberos receptors
Nociceptor	Pain		Free nerve endings
	General chemical sensitivity		Free nerve endings
Magnetoreceptor	Magnetic fields		Photoreceptors (?) Ampullae (?) Trigeminal receptors

in Figure 2-8. Other receptor cells, however, are not modified neurons, but rather are specialized receptor cells; they lack axons and must be innervated by sensory neurons in order for their output to be transmitted to the central nervous system. Hair-cell mechanoreceptors, photoreceptors, and chemoreceptors are among those included in this category of receptor cells. These types of receptor cells are illustrated later in this chapter. Unlike other neurons, which have their cell bodies within the central nervous system, the sensory neurons for most sensory systems have their cell bodies outside of the central nervous system. The cell bodies are nearly always clustered together in a **ganglion**, so named because it resembles a "knot." Ganglia are located just outside of the sensory nerve's point of entry into the central nervous system. They are present in both the spinal nerves, which innervate the body, and some cranial nerves, which innervate the head and neck and also contribute to the autonomic regulation of the viscera. A sensory ganglion is illustrated in Figure 2-9.

Mechanoreceptors

Mechanoreceptors are among the most ubiquitous types of receptors. Although they exist in a variety of forms, their common feature is their response to mechanical deformation,

such as bending, stretching, or twisting. Some mechanoreceptors are involved in the detection of touch or pressure on the body surface. Others respond to stretching such as those in joints, tendons and muscle spindles, and in the digestive system. Still other mechanoreceptors are located at the bases of surface hairs, feathers, and scales and respond when the position of the surface structure is displaced. You can demonstrate this for yourself by lightly running your finger across the hairs on your arm or head without touching the skin surface. The hairs that make up the facial whiskers or vibrissae of mammals are typical of such hairs. Some mechanoreceptors are illustrated in Figure 2-8.

Mechanoreceptors have been best studied in mammals, which possess a large variety of mechanoreceptor types. We know considerably less about the mechanoreceptors of non-mammalian vertebrates. Some amphibians and reptiles are exceptionally sensitive to vibrations of the substrate on which they are situated; they possess cutaneous mechanoreceptors on their ventral skin. Birds have mechanoreceptors on or near the base of their feathers, possibly indicating whether their feathers are close to the body surface (a thermoregulatory mechanism) and/or possibly indicating air speed.

Mechanoreceptors for touch may be classified in several ways. One way is to categorize them according to the speed at

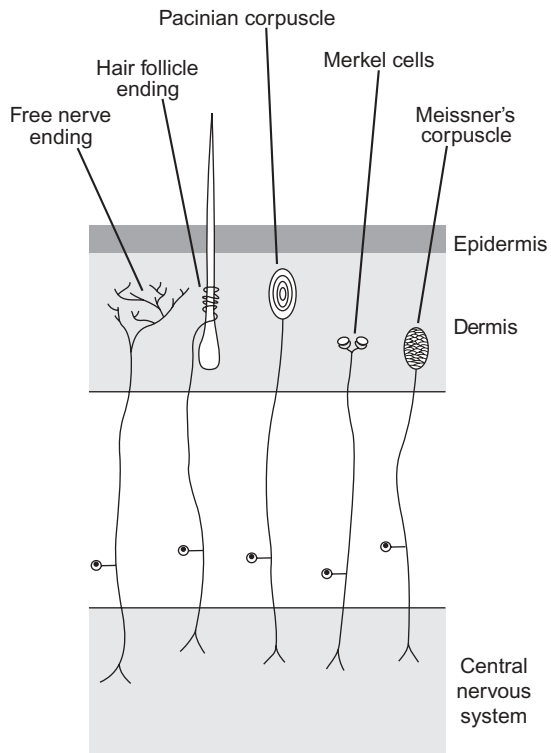


FIGURE 2-8. Examples of somatosensory receptors in the skin.

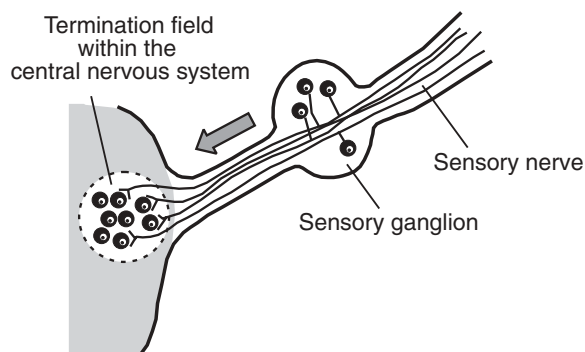


FIGURE 2-9. A sensory ganglion containing the somata of sensory neurons en route to their termination field in the central nervous system. The arrow shows the direction of conduction of the action potentials.

which they adapt to continuous bending or deformation; these are the **fast-adapting** and **slow-adapting** mechanoreceptors. Both types may be further subdivided according to the characteristics of their receptive fields: large with indistinct borders or small with distinct borders.

Hair Cells. A specialized group of mechanoreceptors are the hair cells, which are cells with one or more hairs, or **stereocilia**, protruding from them as well as a longer hair called a **kinocilium**. The stereocilia appear to be involved in the trans-

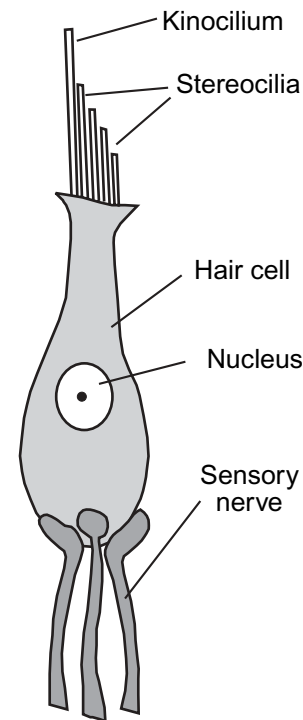


FIGURE 2-10. A hair-cell mechanoreceptor. Hair cells are found in the auditory, lateral line, and vestibular systems.

duction of mechanical energy into a receptor potential, but the kinocilia do not seem to play a direct role in this process. Kinocilia are present in all vertebrates, but in mammals they degenerate during development and hence are not found in adult mammals.

Figure 2-10 shows a typical hair cell. These cells generate receptor potentials in response to bending of their hairs. Hair cells typically are found in fluid-filled chambers, such as the auditory and vestibular organs of the ear and the lateral line organs of the head and the body of aquatic anamniotes. This type of receptor is responsive to displacement waves in the surrounding fluid that have been transmitted from the external environment. The pressure waves that are detected by the lateral line system are of low frequency of the sort that would be produced by the swimming movements of neighboring fish in a school or the bow wave of an approaching predator. Likewise, the hair cells of the vestibular system respond to the low-frequency waves that are set up in the fluids of the vestibular apparatus when the tilt of the head is changed or as the acceleration of the body changes. A third set of hair cells is tuned to respond to the higher frequencies of wave action that occur in the auditory organs when those pressure waves in the external environment that we call "sound" (i.e., pressure waves in the frequency range that we can hear) are transmitted to the fluid in the hearing organ. The external environment may be water, as in the case of fishes, or air, as in the case of terrestrial animals. Indeed, the transition from water to land resulted in dramatic changes in the ear and in hearing mechanisms as a result of the differences in the way sound waves are transmitted through water and air.

The auditory hair cells in tetrapods are located in the inner ear in a structure known as the **basilar papilla**. In mammals, this structure (along with some related structures) is called the **organ of Corti**. The hair cells are arranged in rows in these structures. Some of the hairs are free and others are embedded in an overlying structure. In either case, the pressure of the incoming sound waves ultimately causes these hairs to bend with resulting generator potentials. A more detailed discussion of the mechanics of hearing as well as the variety of hearing organs and their relationships to the animals' environments may be found in the specialized books and articles on this subject listed at the end of the chapter.

Eimer's Organs and the Star-Nosed Mole. The star-nosed mole (*Condylura cristata*) is a mole with a unique sensory adaptation of its snout. The snout consists of a pair of arrays of eleven fleshy, highly mobile, fingerlike protuberances, called rays, that the animal uses to explore the environment (see Box 2-3, Figure 2). Each ray contains thousands of specialized cutaneous mechanoreceptors known as **Eimer's organs**. They are unique to moles and are not found elsewhere among the eulipotyphlans (formerly called insectivores; see Chapter 4)—moles, shrews, and hedgehogs. They are also lacking in moles that live in harsh, very dry climates.

Each Eimer's organ consists of a dome-like swelling of the epidermis below which is located a column of flattened epidermal cells. Contained within the organ are free nerve endings associated with the flattened disks, Merkel mechanoreceptors, and encapsulated corpuscles. The density of Eimer's organs far exceeds the density of touch receptors on even as sensitive a receptor surface as a human hand. This provides the animal with an exceptional somatosensory image of whatever surface the rays are exploring. Because the nasal rays move very quickly, the animals must make very rapid textural discriminations in order to form this tactile picture of the environment immediately in front of its nose.

Lateral Line Organs. An important sense-organ system for aquatic anamniotes are the lateral line organs, which generally are found in the lateral line canals. These canals are located on the head and the body of fishes and larval amphibians. They contain a class of mechanoreceptors known as **neuromasts**, which are hair cell-like receptors. These neuromast receptors are situated in the lateral line organs that line the fluid-filled canals. Some canals are closed and their fluid is internally secreted; others canals have external openings that permit the surrounding water to enter. Neuromasts respond to low-frequency pressure changes in the surrounding water as might

BOX 2-1. Dome Pressure Receptors

The river glides lazily through the dark swamp. Its surface is smooth except for some floating leaves and a half-submerged log. A young deer cautiously approaches the water and begins to drink. Suddenly, the "log" lunges at the deer. Too late the deer sees that the log is a large alligator. How was this predatory attack launched with such surprise and such precision? The answer is with the assistance of a newly characterized but quite ancient sensory receptor called a **dome pressure receptor**. These receptors appear as a series of bumps or small domes on the upper and lower jaws of semi-aquatic alligators and crocodiles above and below the tooth line (see Figure 1) and represent a localized thinning of the animal's body armor.

Daphne Soares discovered that these receptors allow American alligators (*Alligator mississippiensis*) to orient toward their prey, even in total darkness, and without the aid of audition. She observed that single droplets of water dripped onto the surface of the water surrounding the alligator will evoke the orientation response, even in total darkness, as long as the animal's face was positioned at the air-water interface. If the head was above the water's surface, no response occurred. Likewise, if the dome pressure receptors were covered with a plastic elastomer, the alligators failed to respond to the stimulus. Soares reported that the dome pressure receptors are innervated by branches of the trigeminal nerve. (See Box 11-1 for additional sensory receptor types innervated by this versatile nerve.)

In addition to studying the anatomy, physiology, and behavioral functions of the dome pressure receptors, Soares also investigated their phylogeny, as shown in Figure 1, which is a cladogram of crocodyliform reptiles. Examination of the upper jaw, or maxilla, and lower jaw, or mandible, of modern and ancient crocodyliforms revealed a series of small openings, or foramina, through which pass the end branches of the trigeminal nerve. The foramina are arrayed in a hexagonal or "beehive"-shaped pattern. All living semi-aquatic crocodilians possess both the foramina in a beehive pattern and the dome pressure receptors. When Soares examined the skulls of extinct relatives of the modern crocodilians, she found the linear pattern only in those extinct species that are believed to have been adapted to a fully terrestrial environment, such as *Sebecus*. Other ancient crocodilians, such as *Protosuchus*, and modern lizards also all have the foramina in the linear pattern, which supports the idea that the beehive pattern and dome pressure receptors are a unique development of the more recent, semi-aquatic crocodilian lineages. Even the marine iguana, which, like crocodilians, leads a semi-aquatic existence, has the linear pattern and not the beehive pattern of the semi-aquatic crocodilians.

The paleontological evidence, taken along with the behavioral, physiological and anatomical findings suggest that the semi-aquatic crocodilian lineages evolved a unique sensory receptor that enables these large predators to lie in stealth in the water awaiting subtle pressure waves associ-

BOX 2-1. Dome Pressure Receptors—cont'd

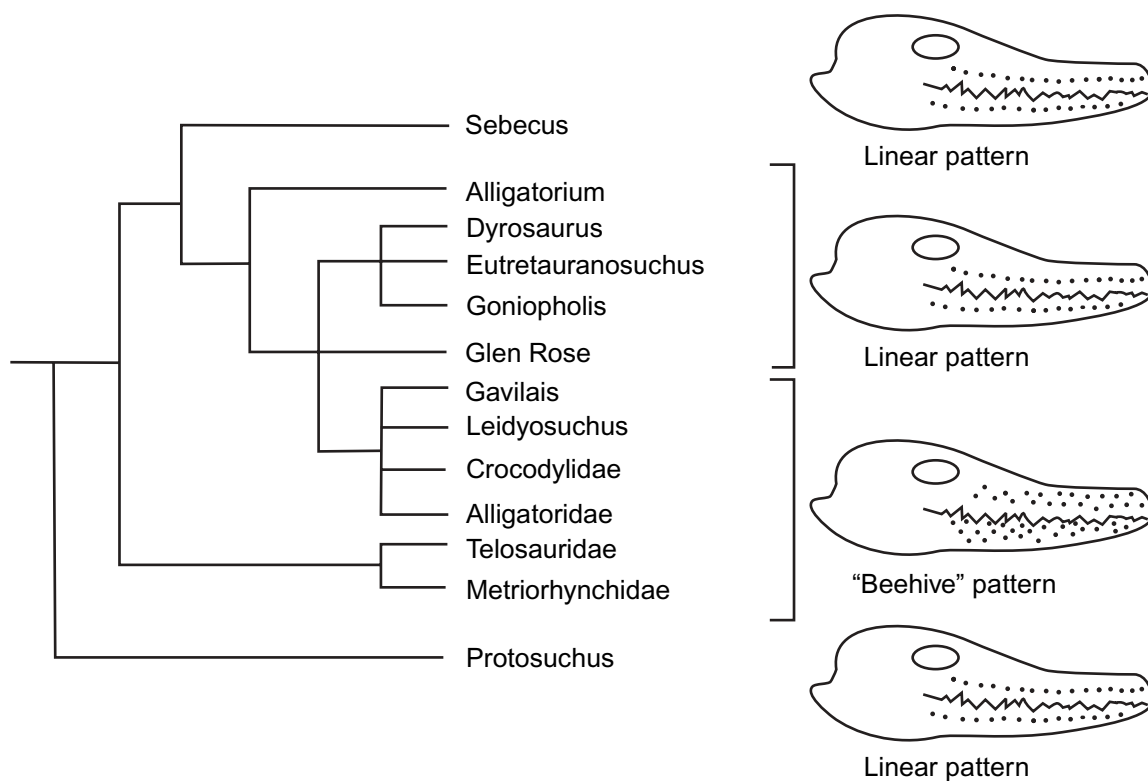


FIGURE 1. A cladogram of crocodyliform reptiles showing evolution of dome pressure receptors, as indicated by the presence of a "beehive" pattern of trigeminal nerve foramina on the upper and lower jaw surrounding the tooth line. The linear pattern is characteristic of the earliest crocodilians and those genera not adapted to the aquatic environment. The linear pattern is also characteristic of lizards, whether or not they are adapted to an aquatic environment. Adapted from Soares (2002) and used with permission.

ated with a disturbance of the water's surface to signal the position and distance of prey, even in total darkness. The ability to process information about the precise location of prey in the water in conjunction with their highly developed locomotor system may have contributed to the long history of success of these animals as predators.

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be produced by the swimming movements of other fish in a school, or by the approach of a predator.

The lateral line canals of a bony fish are shown in Figure 2-11. At least three canals are located on the head, one above the eye (supraorbital canal), one below the eye (infraorbital canal), and one on the lower jaw or mandible (mandibular canal). Additional head canals are present in some fishes. The lateral or trunk canal runs the length of the body.

Radiant-Energy Receptors

Energy that is propagated in the form of electromagnetic waves (or streams of particles called photons) is known as **radiant energy**. A rather narrow portion of the radiant energy spectrum constitutes visible light. Please remember that when we use the term "visible," we mean visible to humans. Various nonhuman animals have no difficulty detecting portions of the

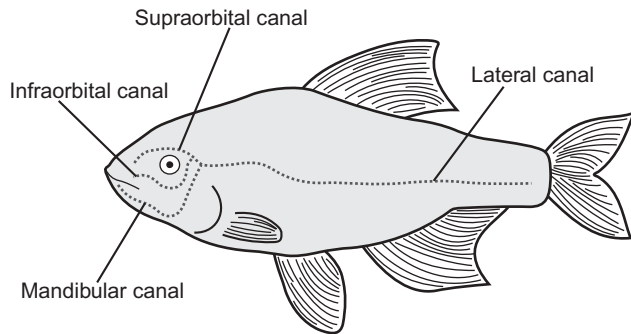


FIGURE 2-11. The lateral line canals of a fish. The main lateral canal runs the length of the body. Three or more canals are located on the head. The figure shows one above the eye (supraorbital), one below the eye (infraorbital), and one on the lower jaw (mandibular).

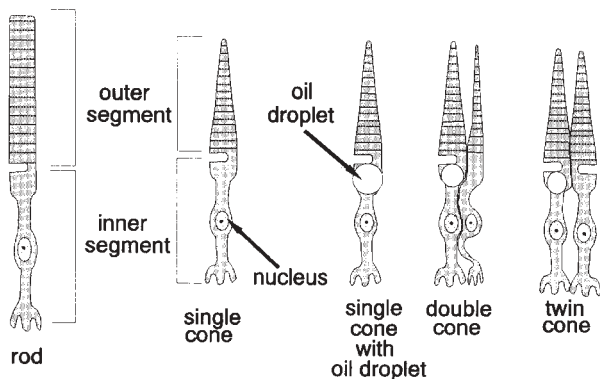


FIGURE 2-12. Photoreceptors of the retina. A rod and several types of cones are shown. The cones of many vertebrates contain colored oil droplets between the inner and outer segments. Vertebrate cones often are paired as may be seen in the double and twin cones.

electromagnetic spectrum that are undetectable to us. Visible light is detected by specialized cells called **photoreceptors**. The two most common types of photoreceptors are the rods and cones of the retina of the eye. These are shown in Figure 2-12. Both types of photoreceptors consist of an inner and an outer segment. The outer segment consists of a series of stacked disks that capture light energy and transduce it into a receptor potential by means of a series of complicated chemical reactions in a group of compounds known as **photopigments**. Each photopigment reacts with light only in a specific range of the spectrum. Rods can be distinguished from cones by the appearance of the stacks of disks; in the rods, the disk diameter remains constant along the length of the outer segment, whereas the diameter of the cone disks becomes progressively smaller so that the cone outer segment tapers to a blunt point. The inner segments of the photoreceptors contain the nuclei and terminal branches of these cells.

In nonmammalian vertebrates, rods and cones can be further differentiated by the presence of oil droplets located between the inner and outer segments of the cones. These

droplets may be colorless or they may be yellow, greenish yellow, orange, or red. They appear to function as color filters that serve to restrict the spectral range of light that reaches the outer segment. Thus, a yellow droplet filters out short wavelength (blue) light and a red droplet filters out wavelengths in the range that we call green.

Figure 2-12 also shows some of the varieties of cones, which can include two types of paired cones: double cones and twin cones. These paired cones are characterized by the close proximity of the partners and the absence of pigment epithelium between their outer segments. The partners of these paired cones function in close coordination with each other because they are linked by fast acting, bidirectional electrical synapses. Moreover, they often are found in clusters. Their close proximity thus appears to be a device for increasing the local density of the photoreceptors, which increases the probability of capturing photons. Paired photoreceptors are not found in mammals.

The Retina. Figure 2-13 shows a diagram of the **retina**. Although we often discuss the retina as if it were a simple sensory surface, the retina is, in fact, a highly complex structure with very sophisticated processing capabilities. Indeed, the retina actually is a component of the central nervous system. A full treatment of the anatomy and function of the retina is beyond the scope of this introductory work, and we can only present some of the main features here.

The retina is the innermost layer of the eye. The outermost layer is the **sclera**, which is the tough coat of the eye that gives the eye its globular shape. The next layer is the **choroid**, which is highly vascular and provides the retina with access to the circulatory system. Deep to the choroid lies a layer of **pigment epithelium**. The tips of the photoreceptors are in contact with the pigment epithelium. As its name implies, the pigment epithelium contains dense pigment granules that exclude light. When the light level is high, the pigment epithelium extends down into the spaces between the outer segments to block excess light from reaching the photopigments. When the light level is low, the pigment epithelium retracts to permit the photopigments to have the maximum opportunity to capture photons.

The retina itself consists of several regions. The layer of photoreceptors is the first stage for the processing of light stimulation. As Figure 2-13 indicates, light must pass through all of the other retinal layers before it reaches the photoreceptor outer segments to begin the process of sensory transduction. The layer of photoreceptor nuclei is known as the **outer nuclear layer**. The next region is the middle retina, which consists of **bipolar cells**, **horizontal cells**, **amacrine cells**, and **interplexiform cells**. The retinal layer that contains the nuclei of these cells is known as the **inner nuclear layer**. The inner retina consists of the layer of ganglion cells, which are the source of efferent axons from the retina to the brain. These axons converge from all parts of the retina to a single location, known as the **optic nerve head**, to form the **optic nerve**. The bipolar cells connect the photoreceptors to the ganglion cells. The remaining cell types modulate the activity in this pathway from photoreceptors to bipolars to ganglions. The layer of the retina in which the photoreceptor terminals contact the dendrites of the bipolar cells is called the **outer plexiform layer**,

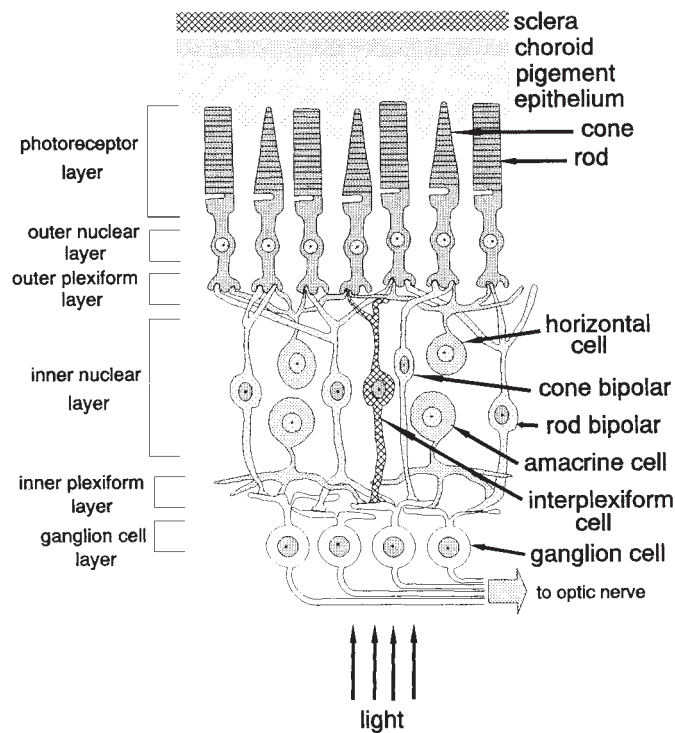


FIGURE 2-13. The retina. The photoreceptors are pointing toward the pigment epithelium, choroid, and sclera. Their outer segments form the photoreceptor layer, their somata form the outer nuclear layer, and their zones of contact with other neurons of the retina form the outer plexiform layer. The inner nuclear layer comprises the somata of the various types of integrative neurons of the retina: the horizontal cells, the bipolar cells, the amacrine cells, and the interplexiform cells. The efferent cells of the retina are the ganglion cells; their dendrites contact the terminals of the integrative cells in the inner plexiform layer. The horizontal cells modulate the activities of the outer plexiform layer, and the amacrine cells modulate the activities of the inner plexiform layer. The two plexiform layers are connected by the bipolar and interplexiform cells. Adapted from Nicholls et al., 1992 and used with permission of Sinauer Associates, with additional information from other sources.

and the layer in which the terminals of the bipolar cells contact the dendrites of the ganglion cells is called the **inner plexiform layer**.

The horizontal cells and amacrine cells provide for lateral interactions within the outer and inner plexiform layers, respectively, while the interplexiform cells link activities between the two plexiform layers. The horizontal cells spread out within the outer plexiform layer to provide a lateral interaction by coupling or uncoupling of the photoreceptors, which permits them to function as groups or as independent detectors of photons. The amacrine cells perform a similar function within the inner plexiform layer. The interplexiform cells provide feedback from the amacrine cells to the horizontal cells and to the bipolar cells.

The Optic Nerve. The bipolar cells project to the **retinal ganglion cells**, which give rise to the axons that form the **optic nerve**. The optic nerve leaves the globe of the eye and passes toward the brain. On route to its terminations in the brain, the optic nerve crosses the midline so that some or most of the axons from the right eye terminate in the left brain and vice versa. This point of crossing is known as the **optic**

chiasm. Once the ganglion-cell axons have crossed the midline in the optic chiasm, they are thereafter referred to as the **optic tract**. Not all of the optic nerve axons decussate (cross the midline) in the optic chiasm. Some axons remain ipsilateral (on the same side) to the eye of origin. The proportion that remains ipsilateral varies considerably across vertebrate classes. In general, however, nonmammals tend to have the overwhelming majority of optic axons crossing to the contralateral (opposite) side. In mammals, the proportion of ipsilateral optic axons can be as much as 50%. This will be discussed in greater detail in Chapter 26.

Centrifugal Axons. Not all of the axons in the optic nerve travel from the eye to the brain. In the optic nerve, as in all sensory cranial nerves, centrifugal axons are present that pass from the brain to the receptors. These centrifugal axons generally suppress the activity of the receptors and may play a role in attention mechanisms.

The Median Eye. The eyes that we have been discussing thus far may be considered lateral eyes in that they are located more or less at the sides of the skull. The optics of these eyes

typically are adapted to forming detailed images of the external world on the retina. A considerable amount of this detail is represented in the neural signals that are transmitted to the brain. In addition to these lateral eyes, some vertebrates (but not mammals) have a single, unpaired median eye, located at the top of the skull. This median eye is known as the **pineal eye**. Because the pineal is also known as the **epiphysis**, one could refer to this eye as the **epiphyseal eye**. Unlike lateral eyes, median eyes are not designed to form images, but merely to gather light. The median eye usually consists of a layer of photoreceptors that send their axons directly to the brain. Median eyes do not have the additional neuronal elements that are found in the retina, and therefore are greatly limited in their ability to transmit information about the spatial properties of the visual world. In some vertebrates, a second median eye is present just below the first. The second eye is known as the **parapineal eye** or **paraphysis**. Frequently, the median eye is found below a translucent patch of skin that permits diffuse light to reach the photoreceptors. In some vertebrates, however, a lens-like element occurs that aids in the collection of light.

The median eye synthesizes the hormone and neuroactive substance **melatonin** from serotonin in the absence of light. Melatonin is involved in daily biological rhythms and in seasonal rhythms that depend on the progressive lengthening or shortening of the day, metamorphosis, color change, and sexual development. In birds and mammals, the epiphysis is glandular (the pineal gland) and produces melatonin. It retains its sensitivity to light, even though the light-dark cycle is mostly regulated through central nervous system pathways. Figure 2-14 shows a median eye, from which the axons terminate in the brain.

Pit Organs. Another type of radiant energy detector is the pit organ, which is found in a group of venomous snakes known as “pit vipers.” Rattlesnakes and the other pit vipers have a sensory pit that is located on the snout between the lateral eyes and the nostrils. Certain nonvenomous snakes, such as boas and pythons, have rows of pit organs located on their upper and lower lips. Suspended between the inner and outer cavities of the sensory pit is a membrane that consists of a type of photoreceptor that is sensitive to the infrared range of the electromagnetic spectrum. Infrared is invisible to the human eye, but it can be felt on our skin as heat. In contrast to the heat receptors of the skin, however, the pit membrane is extremely sensitive to subtle differences between the infrared radiation coming from an object (such as a small mammal) and that coming from the background. The pit membrane is innervated by sensory axons of the trigeminal nerve (see Chapter 11). A pit organ is illustrated in Figure 2-15.

Chemoreceptors

Chemoreceptors sense the chemical properties of the environment. A common feature among chemoreceptors is that they are capable of being stimulated by certain classes of water-soluble chemicals. The two chemosenses that humans are familiar with are gustation (taste) and olfaction (smell). In water, these senses act both as distance receptors (i.e., they can detect stimulus sources that are remote from the receptor,

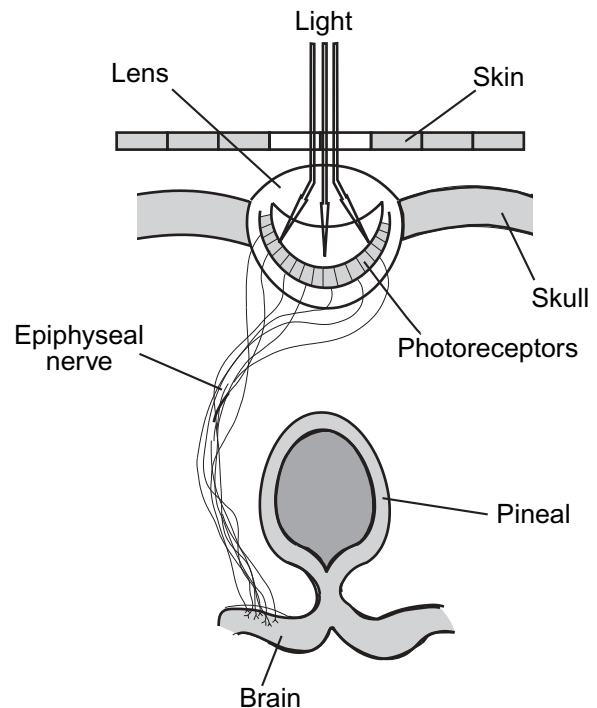


FIGURE 2-14. An example of a median eye. Light impinges on the photoreceptor layer, which is the origin of the epiphyseal nerve that terminates in the epithalamus near the pineal (epiphysis).

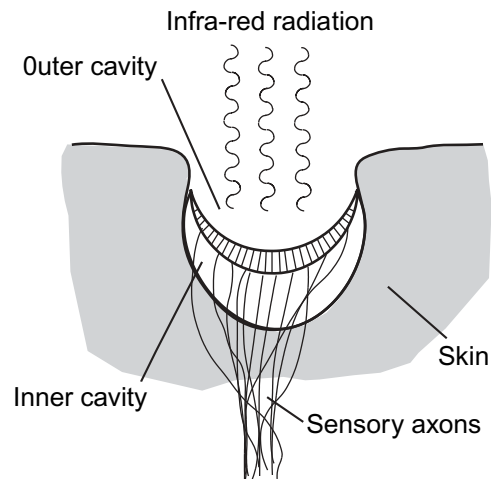


FIGURE 2-15. An IR pit receptor. An IR-sensitive membrane is suspended between the inner and outer cavities of the sensory pit. The membrane is innervated by sensory axons of the trigeminal nerve.

similar to hearing and vision) and as contact receptors (i.e., they detect stimuli that are in direct contact with or very close to a body surface as do touch, temperature, and pain receptors). This occurs because the chemical stimuli must be soluble in the water surrounding the animal. For animals that live in air, however, only the olfactory sense maintains its dual role as both a distance sense and a contact sense. Gustation, on the

other hand, is only a contact sense in land animals because the taste stimuli are only soluble in water, not in air; these stimuli can only produce taste sensations when they dissolve in the epithelial coating of the taste buds within the oral cavity.

Gustation. The gustatory receptors are located within structures known as **taste buds**. In tetrapods, which have tongues, the taste buds are located mainly on the tongue, although some are in the throat as well. The muscular tongue evolved in those branches of the vertebrate lineage that left the water and adapted to life in air where there is no convenient column of sucked-in water to carry food from the mouth to a point where it could be swallowed into the digestive system. The tongue serves this purpose in land animals. In frogs and some reptiles, it serves to grasp prey and bring them quickly into the mouth. In the remaining tetrapods, the tongue serves to manipulate food once it has entered the mouth.

In nontetrapods, taste buds not only are located in the mouth, but also in the throat, on the head, and, sometimes, as in carp, all over the body surface. Some fishes, such as the catfishes, have evolved facial appendages (that give these animals their name) that are studded with taste buds. These appendages, known as **barbels**, are used to sample the gustatory qualities of the environment in the search for edible objects. A catfish typically has more than 100,000 taste buds. Other fishes have fewer but still quite substantial quantities.

The number of taste buds varies among different vertebrate classes. Fishes may have many thousands or even hundreds of thousands of taste buds. Among the land vertebrates,

birds have the fewest taste buds and mammals have the greatest numbers. Even within classes, the number varies considerably. Thus, among mammals, humans have approximately 10,000 taste buds (90% of which are on the tongue), in contrast to rabbits and some ungulates (hoofed mammals), which can have two to three times that number.

Figure 2-16 shows a taste bud with its taste receptors. Taste receptors typically are located within a **gustatory papilla**, which can be a raised structure or a pit with a pore opening to the outside. The walls of these papillae contain small, barrel-shaped structures, which are the taste buds. Each taste bud contains dozens of taste receptor cells.

The primary taste qualities of humans are “sweet,” “sour,” “salt,” and “bitter.” Other more complex tastes are possible from combinations of these. Taste, however, must be distinguished from *flavor*, which is what most people mean when they refer to the “taste” of something. For example, “this tastes like chocolate” or “this tastes exactly like the way my mother cooked it.” These sentences really mean that something had the flavor of chocolate or had the same flavor as Mom’s recipe. The reason that this distinction is necessary is because flavor is a different chemosense than taste; the experience of flavor results from a combination of taste and smell. We are all familiar with the loss of the flavor of food when we have a bad cold with a stuffy nose. We may complain that nothing seems to have any “taste” in such a circumstance, but in fact our sense of taste (sweet, sour, salty, and bitter) is perfectly intact. What has occurred is that olfactory stimuli from the mouth (or from the external world, for that matter) cannot reach our olfactory receptors.

BOX 2-2. Another Taste System?

In addition to the classical taste system, which uses gustatory cells within taste buds as the receptors, an additional chemosensory cell type has been reported on skin surfaces, in the mouth, and on the gills of anamniotes, including hagfishes, various teleosts, and amphibians. In the latter, they are located on the ventral skin. These cells are called **solitary chemoreceptor cells**, and they are typically, but not always, found in the company of classical taste buds.

Solitary chemoreceptor cells are particularly well developed in two teleost genera—*Ciliata* (rocklings) and *Prionotus* (sea robins), in which they are located on the fins. In *Ciliata*, these cells respond to fish body mucus and also to fish bile. They thus may serve in the detection of predators and/or competitors. In *Prionotus*, the cells are located on the pectoral fins, which explore the bottom, and may be involved in feeding. They may have other chemosensory functions as well.

Recently, solitary chemosensory cells have been reported in mammals in the gustatory system, the digestive system, and the respiratory system. In newborn rodents, for example, solitary chemosensory cells have been found in the gustatory epithelium. In rats and mice, they have been reported in the nasal epithelium where they form synaptic

contacts with endings of the trigeminal nerve. Interestingly, these receptor cells are responsive to substances that produce a bitter taste in humans and very likely activate trigeminal protective reflexes in response to potentially noxious compounds that enter the nasal air stream. The presence of gustatory receptors in association with the trigeminal nerve is yet another example of the extreme versatility of the sensory division of this cranial nerve (see Box 11-1).

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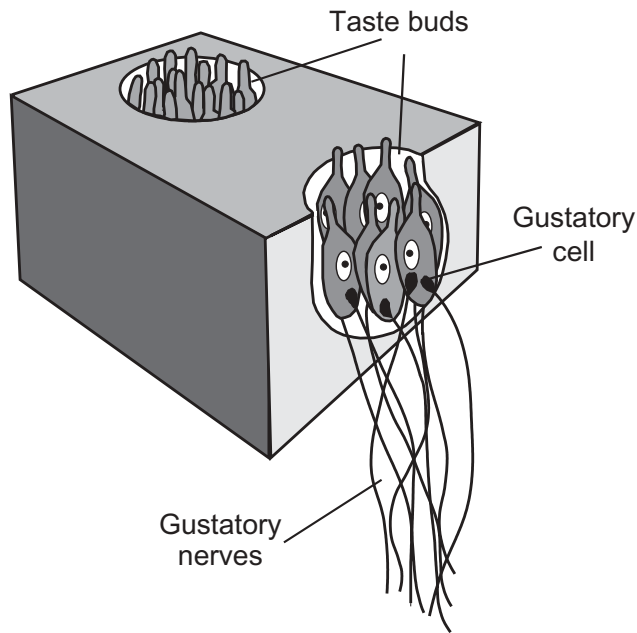


FIGURE 2-16. Taste buds. The cut-away view on the right reveals the structure of the taste bud.

Gustatory neurons in nonhuman land vertebrates respond to the same or similar chemical compounds that produce the human taste qualities; among these are sugars (sweet), acids (sour), salts (salty), and alkaloids (bitter). Gustatory neurons in aquatic vertebrates respond to these same classes of chemical compounds, but in addition respond to a wide range of amino acids. We can only guess at what the subjective gustatory effect of mixing amino acids with the other taste chemicals in varying proportions might be. Whether the subjective experience of these animals to these chemicals is the same as ours, we cannot know, but it is entirely possible that some or all of them may differ. We do know, however, that carbohydrates generally have a sweet taste to us, and both humans and animals will accept carbohydrates as food items. We further know that many plant alkaloids are toxic, that alkaloids evoke a bitter taste in humans, and that animals and humans generally reject bitter tasting food items. Goldfish have been reported to sort out food pellets laced with the bitter (to humans) alkaloids caffeine or quinine from unadulterated pellets using a special oral-particle sorting apparatus (called the palatal organ) contained within their oral cavities.

A fifth taste sensation has been reported in humans; this is known as *umami*. This taste sensation is associated with the food enhancer, monosodium glutamate (MSG). In mice and fishes, taste receptors respond to glutamate, although L-aspartate and other amino acids have been described as evoking umami as well.

Gustatory sensations are not uniformly distributed on the surface of the tongue. Figure 2-17 shows a schematic diagram of a human tongue with the zones that represent the locations of the various taste sensations of humans: sweet (tip), salty (anterior sides), sour (posterior sides), and bitter (back of the tongue). Note the overlap of some of the taste zones. Figure 2-

17 also shows the relative distributions of taste buds on the body surface of a catfish. The darker the shading, the greater the density of taste receptors. Note the presence of taste receptors on the fins and the very high concentrations of receptors on the barbels, the head, and the snout.

Olfaction. Olfactory stimuli are very complex. They emanate not only from food objects but from a variety of sources. Because humans are **microsmatic**, which means that we have a relatively poor olfactory system, we cannot appreciate the rich and complex olfactory world of the **macrosmatic** animals, which have well-developed olfactory systems. The canidae, which include dogs, wolves, coyotes, and other dog-like animals, for example, are macrosmatic, and their abilities to identify individuals by smell are well known.

Olfactory receptors are located in cavities within the nose. The openings of the nose (the nostrils, or nares) allow the medium of the external environment (air or water) into the nasal cavity. Within the cavities is the olfactory epithelium that contains the olfactory receptors. These cavities, however, cannot be blind sacs, which would inhibit the continuous flow of the medium from bringing a smooth and continuous sampling of the external environment to the olfactory epithelium. They therefore have both an anterior and a posterior opening. In fishes, the water flows into the anterior naris, through the nasal sac, and out the posterior naris. Figure 2-18 shows the inflow and outflow of the water column through the anterior and posterior naris. Within the nasal sacs of fishes is a highly folded surface that contains the olfactory receptors. This folding greatly increases the receptor surface area permitting a greater number of receptors to be packed into a small space. In tetrapods, however, the air column is pulled into the nares during the inspiration phase of the respiratory cycle and drawn down into the lungs (Figure 2-19). Openings in the ethmoid bone, which forms the roof of the nasal cavity, lead to the olfactory epithelium. Special bones within the nasal cavity called **turbinate bones** ensure a sufficient turbulence of the air column so that the volatile molecules can reach the olfactory epithelium. The olfactory epithelium is coated with mucus into which protrude the olfactory receptors. Olfactory stimuli (or odorants) are chemical substances that can dissolve in the mucus. Unlike the relatively small number of categories of taste stimuli, the number of odorant categories is vast.

The axons of the olfactory receptors terminate in the **olfactory bulb**, which is a specialized olfactory region of the brain that lies directly above the ethmoid bone. Macrosmatic animals have large, well-developed olfactory bulbs; microsmatic animals have small, less-well-developed olfactory bulbs. Figure 2-19 also shows how the olfactory receptor cell axons pass through the ethmoid bone to terminate in the overlying olfactory bulb.

Vomerolnasal Organ. An important part of the olfactory world is the social aspect. One facet of this is the recognition of individuals, as mentioned above. Another facet of social olfaction is chemical signaling or communication. Many animals signal danger or readiness to mate or mark their territories by means of a class of chemical-communication substances called **pheromones**. A pheromone is a chemical substance secreted by one animal that produces a specific

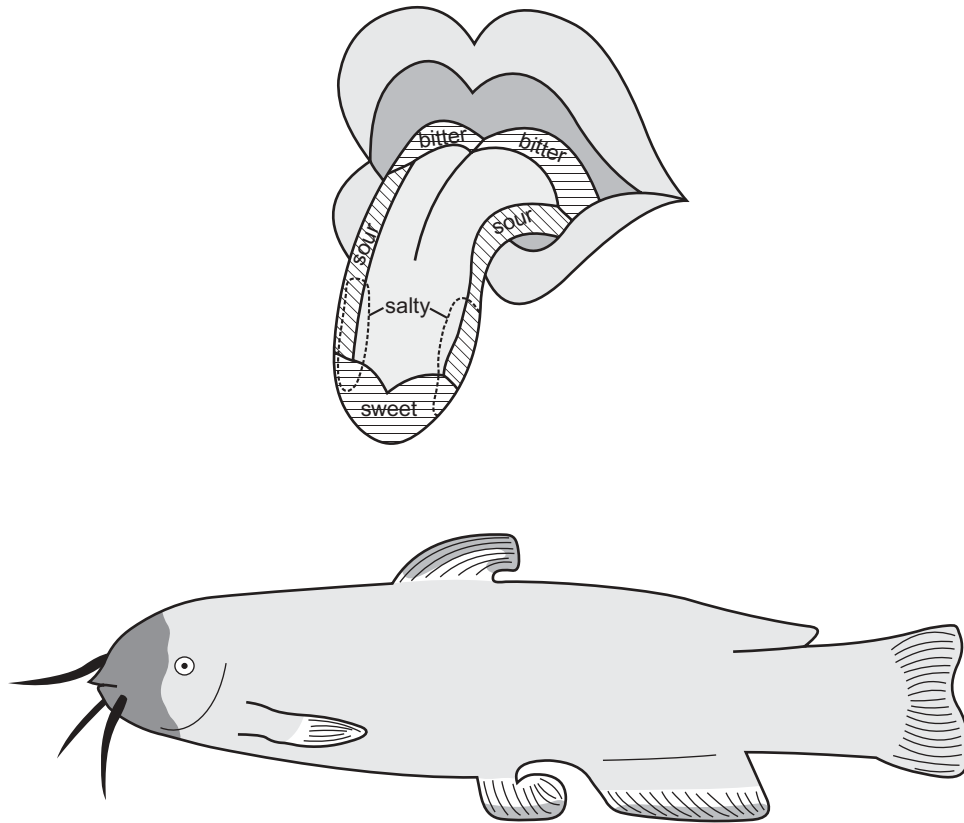


FIGURE 2-17. Top: The taste zones of a human tongue. Receptors that respond primarily to sweet are located at the tip of the tongue. On the sides, just behind the sweet zone, are the salty and sour zones. The bitter zone is located at the rear of the tongue. Note the overlap in the taste regions. Bottom: The relative distribution of taste buds on the body of a catfish. The taste buds are indicated by shading. Greater concentrations of taste receptors are shown by darker shading. Based on data from Atema (1980).

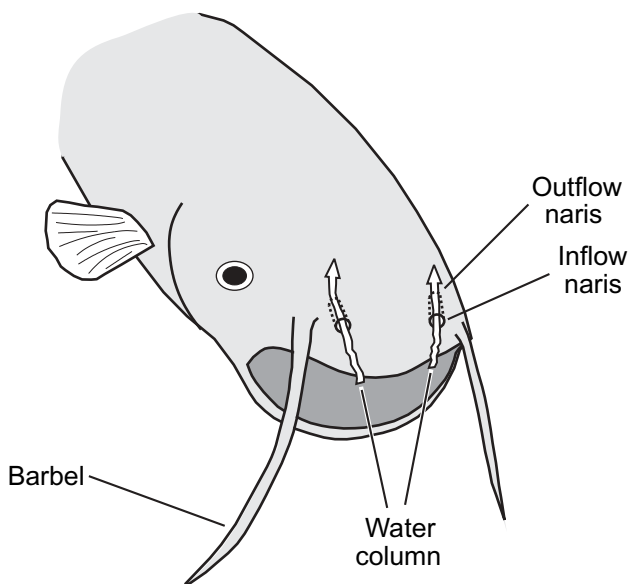


FIGURE 2-18. The nares (nostrils) of a catfish. A column of water enters the anterior naris, passes over the olfactory receptor sheet, and exits through the posterior naris. The barbels of the catfish are covered with taste buds as is much of the rest of its body surface.

behavioral reaction in another animal. Alarm pheromones indicate some dangerous situation, and sex attractant pheromones help males to locate sexually receptive females. Humans normally do not detect sex-attractant pheromones that are secreted by the bodies of other humans, although a few subtle exceptions have been noted. Instead, we rely on a group of chemicals produced by human commercial manufacture known as perfumes.

In some amphibians, some reptiles, and many mammals, the chemoreceptors for pheromones are located in the nasal cavity. However, in a number of vertebrate classes, these chemoreceptors are located in a separate cavity that is in the roof of the mouth and known as the **organ of Jacobson**. Because this cavity is located in a bone known as the vomer, the organ of Jacobson is frequently known as the **vomerolnasal organ**. The vomerolnasal organ is especially well-developed in snakes and some lizards, but absent in turtles; the rapid flicking in and out of the tongue serves to capture olfactory molecules and to bring them in contact with the vomerolnasal organ on the roof of the mouth. Likewise, many ungulates curl their upper lips and inhale air. This behavior, known as the *flehmen* response, serves to draw air over the entrance to the vomerolnasal organ. Figure 2-20 shows a vomerolnasal organ in a reptile.

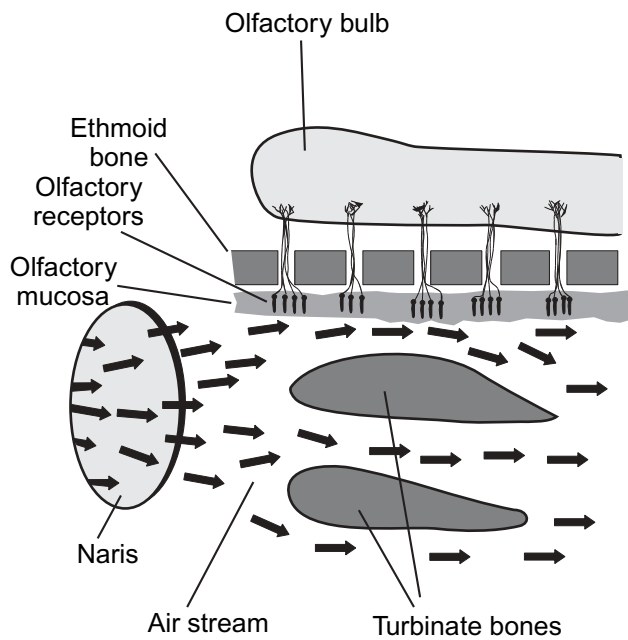


FIGURE 2-19. The olfactory organs of a tetrapod. A stream of air enters the nasal cavity from the outside. The air flows across the turbinate bones and comes in contact with the olfactory receptors located in the mucus layer below the ethmoid bone. The axons of the olfactory receptors pass through openings in the ethmoid bone and terminate in the overlying olfactory bulb.

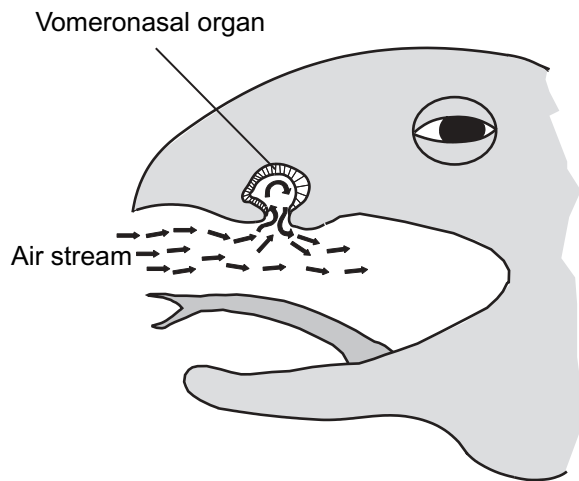


FIGURE 2-20. The organ of Jacobson or vomeronasal organ in a lizard. The flicking of the animal's tongue conducts the air stream into the vomeronasal organ, which is located in the vomer bone of the roof of the mouth. The vomeronasal organ detects pheromones, which are olfactory stimuli that can function as chemical-communication signals.

Primates have a vomeronasal organ during embryological development, but it becomes progressively reduced in size so that by birth it appears to have disappeared. Recent reports, however, indicate that a small vomeronasal organ is present in adult humans. Whether it has neuronal connections to the

brain or whether chemical stimulation of it has any behavioral consequences is unknown at present.

Unlike the olfactory receptors of the nasal cavity, those of the vomeronasal organ do not have cilia extending into the mucus that covers the receptor surface. A further difference between the nasal and vomeronasal systems is that they have different terminations within the brain. The nasal receptors terminate in a part of the brain known as the olfactory bulb (or sometimes as the **main olfactory bulb**), whereas the vomeronasal receptors terminate within an **accessory olfactory bulb** located near the main olfactory bulb.

Nervus Terminalis: An Unclassified Receptor

Still another type of receptor, the functions of which have not yet been established, is the **nervus terminalis** or terminal nerve, a microscopically small nerve that innervates the nasal septum. This nerve is present in all jawed vertebrates. Unlike the nasal and vomeronasal systems, the terminal nerve has no specialized receptor endings but rather ends in free nerve endings. Because many of the axons of the terminal nerve contain the hypothalamic hormone, GnRH (gonadotropin releasing hormone), which is involved in a number of reproductive neuroendocrine processes, the terminal nerve may function, among other things, in the detection of pheromones, especially in those vertebrates in which a vomeronasal organ is not present, although this has not been demonstrated experimentally. The terminal nerve also may detect temperature changes or other nonchemical, intranasal stimuli.

Electroreceptors

The detection of electric fields is widespread among vertebrates. Some aquatic predators can detect the electric fields produced by the contractions of the muscles of their prey as they swim. Even the electric fields produced by the contractions of the muscles of respiration may be sufficient for predators to detect at a short distance. Although predatory electroreception is typical in certain groups of cartilaginous fishes and ray-finned fishes, recent investigations report electroreception in lampreys, some amphibians, and in monotreme mammals as well; both platypuses and spiny anteaters have been reported to have electroreceptors in the skin of their snouts.

In addition to detecting the movements of prey, several groups of animals are capable of detecting the self-generated electric fields around their own bodies. These electric fields are much larger than those produced by routine muscle contraction. Rather, they are produced by special organs known as **electric organs**. You probably have heard of the electric eel that is capable of delivering a powerful electric shock to stun or kill prey or animals that threaten it. This powerful electric discharge is produced by electric organs. Other fishes are also capable of powerful electric organ discharges, such as the electric catfish, a ray-finned fish, and the torpedo, a cartilaginous fish from which the undersea weapon gets its name. These fishes, however, do not use their electric-organ discharges only for predation and defense; they also use them to detect objects in the environment around them. They do so by emitting weak

electrical discharges all the time and sensing the distortions of the electric fields surrounding them that result from the presence of nearby objects with high or low electrical conductivity. Objects that conduct electricity well, like other fishes, distort the electric field differently than do poor conductors, such as rocks.

The detection of these weak, self-generated electric fields also is the specialty of several families of ray-finned fishes that are not capable of generating the strong discharges necessary for predation and defense. These animals use their electroreception of changes in the fields around them to locate food, but in a manner quite different from those animals that do not have electric organs; rather than locating prey by the electric fields that emanate from the prey, the weakly electric fishes detect prey by the effects on the electric fields that they generate themselves. In addition to predation, these electric-organ fishes use their electroreception to detect others of their species, to maintain space around themselves, to identify individuals and potential mates, and for other aspects of social behavior. Some electric fishes also can detect the movement-generated electric fields around their prey. Figure 2-21(B) illustrates how stimuli of either high- or low-electrical conductivity affect the lines of the electrical fields actively generated around a weakly electric fish. Figure 2-21(C) shows a shark, which is using its predatory electroreception to detect the electric fields around a fish that it is about to capture.

The electroreceptors themselves fall into two broad categories, each with several subtypes: **ampullary receptors** and **tuberous receptors**. Figure 2-22 shows examples of these two types of receptors. The electroreceptors of fishes are found in

the lateral line canals and are innervated by branches of the lateral line nerves. The independently evolved electroreceptors of monotremes are located in the snout region and are innervated by the trigeminal nerve (see Box 11-1).

The ampullary and tuberous receptors differ in their sensitivity and function. The ampullary receptors are responsive to the sorts of low-frequency electric rhythms that would result from the muscular contractions of respiratory or swimming movements (0.1–50 cycles per second). Tuberous receptors, on the other hand, have a much higher frequency range (50–200 cycles per second), which is the frequency range of the electric-organ discharge. Further details about electroreceptors and electroreception may be found among the references at the end of this chapter.

Nociceptors

The term **nociception**, the detection of something unpleasant, is derived from the same roots as the word “noxious” and generally refers to pain “receptors” that usually are free nerve endings. These are activated when the tissue is cut, crushed, or otherwise damaged. Another type of noxious sensation arises from the stimulation of certain irritating chemicals such as strong acids, bases, and a variety of irritants and toxins produced by animals and plants as a defense against predation or as a form of predation, such as insect bites or jelly-fish stings. Many of the spicy foods activate general chemical sensitivity in the oral cavity. This sensitivity is not limited to the mouth region, however, as anyone can testify who has been eating highly spiced food with their fingers and then makes the

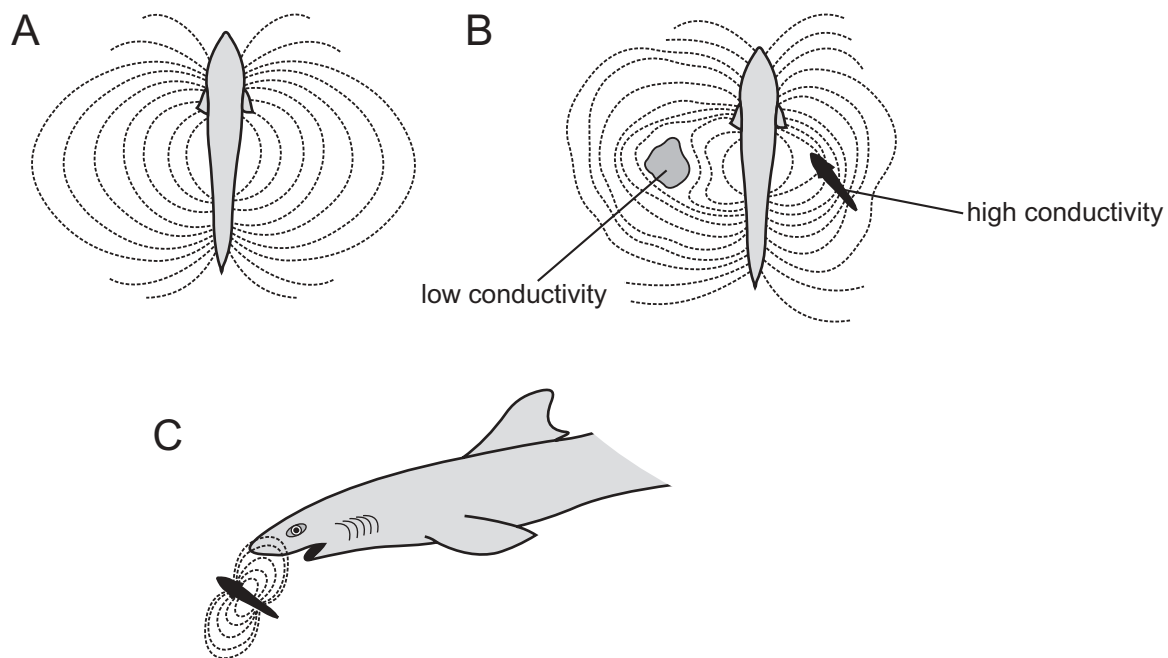


FIGURE 2-21. (A) Actively generated lines of current around a weakly electric fish. (B) Distortion in the current lines as a result of a nearby object of high conductivity (right) and another of lower conductivity (left). Based on Feng (1991) and used with permission of John Wiley & Sons. (C) A predatory electroreceptive shark detects the lines of current around a nearby prey fish. Based on discussion by Kalmijn (1988).

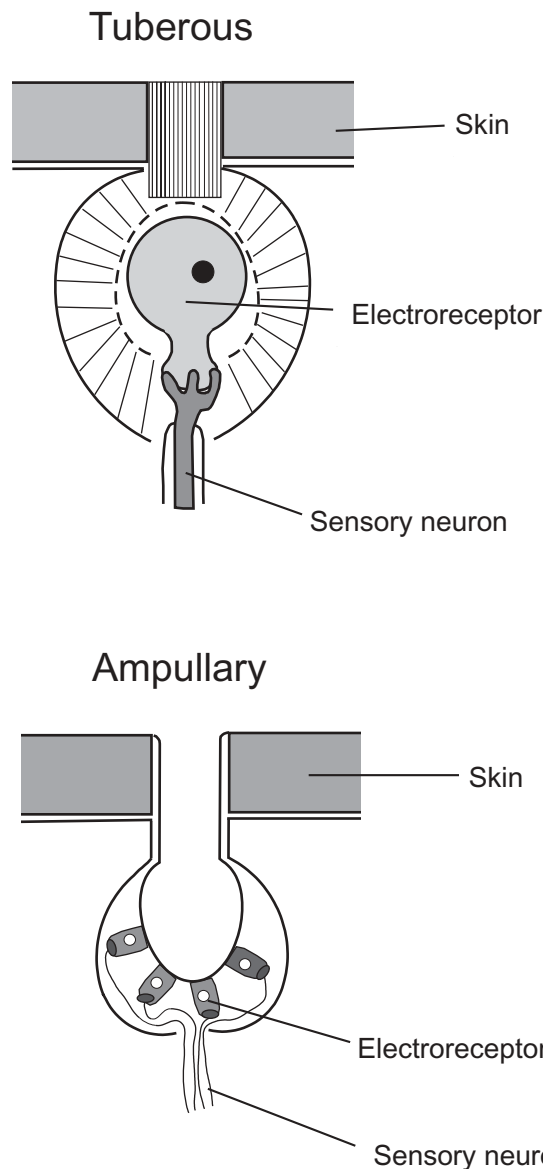


FIGURE 2-22. Two types of electroreceptors: tuberous (top) and ampullary (bottom). Adapted from Feng (1991) and used with permission of John Wiley & Sons.

mistake of rubbing their eyes with their spice-laden fingers. This type of general chemical sensitivity is quite different from chemoreception because receptors are specialized for specific categories of chemical compounds and thus unique sensory experiences resulting from these different compounds do not occur. Like pain, general chemical sensitivity is mediated by free nerve endings located under the surface of the skin and in a number of internal organs.

Magnetoreceptors

Behavioral studies have reported that a variety of vertebrates appear to be able to detect various aspects of the earth's magnetic field that they use for orientation and/or navigation; that is, to go in a particular direction and/or to get from one

place to another on the surface of the planet. For example, attaching small magnets to the heads of homing pigeons interferes with their ability to find their way home. Although the evidence for magnetoreception is convincing, where these receptors are and what they might be remains a mystery. One recent intriguing possibility that currently is being investigated is that the photopigment molecules of the retinal photoreceptors of birds become magnetized, which permits the bird to "see" the orientation of the magnetic field. Other studies have identified magnetic materials in the beak area of some species of birds and reported that a branch of the trigeminal is responsive to magnetic fields. Some investigators have reported that cartilaginous fishes also can use their electroreceptors to detect the electric fields that are produced in their bodies when they swim through the earth's magnetic field the way that an electric current is produced when a coil of wire is moved around a magnet. (See Boxes 11-1 and 18-1 for additional information about magnetoreception.)

TOPOGRAPHIC ORGANIZATION

Another important feature of sensory systems is **topographic organization**, which means that the spatial organization of the receptor surface, such as the skin, the retina, or the basilar papilla, is preserved within the sensory parts of the central nervous system. In the case of the representation of the body in the central somatosensory system, those neurons that receive sensory information that originates on the body surface are organized in a sequential arrangement that roughly mirrors the sequence in which the individual parts are found on the body surface. Thus, head and forelimb representations are at one end of this area, while pathways that originate in the hind limb and tail areas are located at the other end. Within the body representation, the upper trunk is located near the head and forelimb representations and the lower trunk near the tail and hind limb representations.

Sometimes the topographic organization is crude so that only gross areas are represented; other topographic organizations have a very precise point-to-point mapping of the receptor surface within the brain. For example, in those mammals with facial vibrissae (whiskers), each whisker can have its own region of representation in the head area of the somatosensory brain. In general, the more an animal makes use of a sense to detect the fine details of the environment, whether it be small objects in the visual world, subtle acoustic changes in the auditory world, or microvariations in the objects that are touched, the more likely it is that the central representation of the receptor surface will be topographically organized. Moreover, the greater the degree to which a sense is used by an animal, the greater will be the size of the topographic map.

Special names are used to characterize topographic organization within the various senses: the central representation of the retinal map is known as a **retinotopic** organization, and the central representation of the body map is a **somatotopic** organization. In the auditory system, the spatial distribution of the basilar papilla or cochlea is a representation of the different frequencies of sound that the animal can detect, with the low tones at one end and the high tones at the other. The preservation of this spatial mapping of tones is known as a

tonotopic organization. Figure 2-23 shows examples of two receptor surfaces and their corresponding central representations. In the retinotopic organization, although the tectal map appears to have flipped over (due to optic tract geometry), the individual quadrants of the retinotopic map are in the same relationship to each other as they are on the retina. In highly visual animals, within each quadrant a point-to-point mapping of the retina to the retinotopic map exists. The somatotopic map of the digits and the palm (shown in Box 2-3, Fig. 1B) also is in the correct sequence and forms a virtual map of the surface of the paw. Finally, the order of frequencies present in the auditory receptor surface is preserved within the brain. Topographic organizations may be found in any sensory system in which the ordering of either the position in space or specific sensory qualities is important to the animal's success in its environment. Thus, in animals in which gustation and olfaction are highly developed, evidence for chemotopic maps has been reported. For example, each taste-bud studded barbel (or whisker) of the catfish has its own area of representation within the central gustatory system of this animal. The olfactory bulb, however, appears not to be coded according to olfactory space, but rather is organized according to odor categories. Olfactory space would have to be represented by intensity differences between the two olfactory bulbs, much as auditory space is represented by intensity, time of arrival, and other acoustical differences between the two ears.

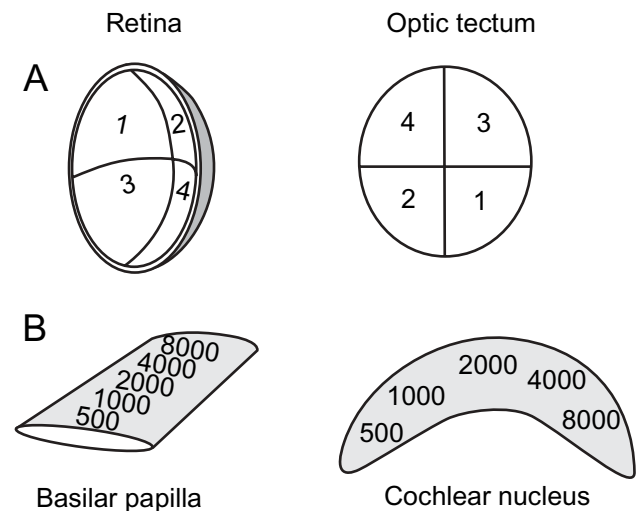


FIGURE 2-23. Topographical organization in the visual and auditory systems. (A) Retinotopic organization: A topographical representation of the retina on the optic tectum in a reptile. (B) Tonotopic organization: A topographical representation of the basilar papilla on one of the cochlear nuclei of a bird.

BOX 2-3. Isomorphic Topographic Maps

An examination of the topographic maps in Figure 2-23 might suggest to the reader that these maps actually form a kind of picture of the sensory surface within the nervous system. In many instances these maps do form an impressive representation of the sensory surface within the brain. Although most of these detailed topographic maps are located in the cerebral cortex of mammals, they also occur in other vertebrate classes as well. Figure 1 shows examples of four such highly precise topographic maps. William Hodos and Ann Butler have termed such precise representations of the sensory surface **isomorphic maps**. Isomorphic maps give the most spatially detailed representation of the sensory surface of any topographic maps. They are the hallmark of a highly developed, sophisticated sensory system.

On the left side of the figure is a cartoon of the sensory surface; on the right side is a map of the neural representation of that sensory surface. In the figure, the left side of part A represents the snout of a rodent with its array of vibrissae (whiskers) and the right indicates the representation of the snout region on the somatosensory cortex of the brain. Within the snout region, each vibrissa has its own representation known as **barrels**, but the overall organization of the barrels within the snout region is a close representation of the location of the vibrissae on the animal's snout.

Part B shows the ventral surface of the paw of a raccoon, an animal with excellent ability for fine manipula-

tion of objects with its paws. In the figure, the digits have been indicated by numbers and the palm pads by letters. Note that the somatosensory representation of the paw matches the sensory surface in an isomorphic manner. Part C represents "whiskers" of another kind, the so-called whiskers of a catfish, which give the animal its name. These structures are unrelated to the vibrissae of mammals, although they do have some functions in common as organs for exploring the close-by environment. Catfish "whiskers" are known as **barbels** and are used for exploring the chemical attributes of the substrate below the fish. This catfish has four barbels on each side—a nasal barbell adjacent to the naris (NB), a maxillary barbell on the upper jaw (MX), and two mandibular barbells, a lateral (LM) and a medial (MM), on the lower jaw. The axons associated with the barbel gustatory receptors terminate in a region of the fish's hindbrain known as the **facial lobe**. Within the facial lobe is an isomorphic representation of these barbels. The region labeled TTL indicates the area devoted to the representation of the taste buds from the rest of the body.

Finally, we come to an extreme example of isomorphic mapping of a sensory surface. Part D of the figure shows a cartoon of the snout region of a star-nosed mole. A sketch of the entire animal is shown in Figure 2. As reported by Kenneth Catania and Jon Kaas, each half of the rostral end of the animal's snout contains 11 fleshy finger-like protuberances known as **nasal rays**. The two black spots in the

BOX 2-3. Isomorphic Topographic Maps—cont'd

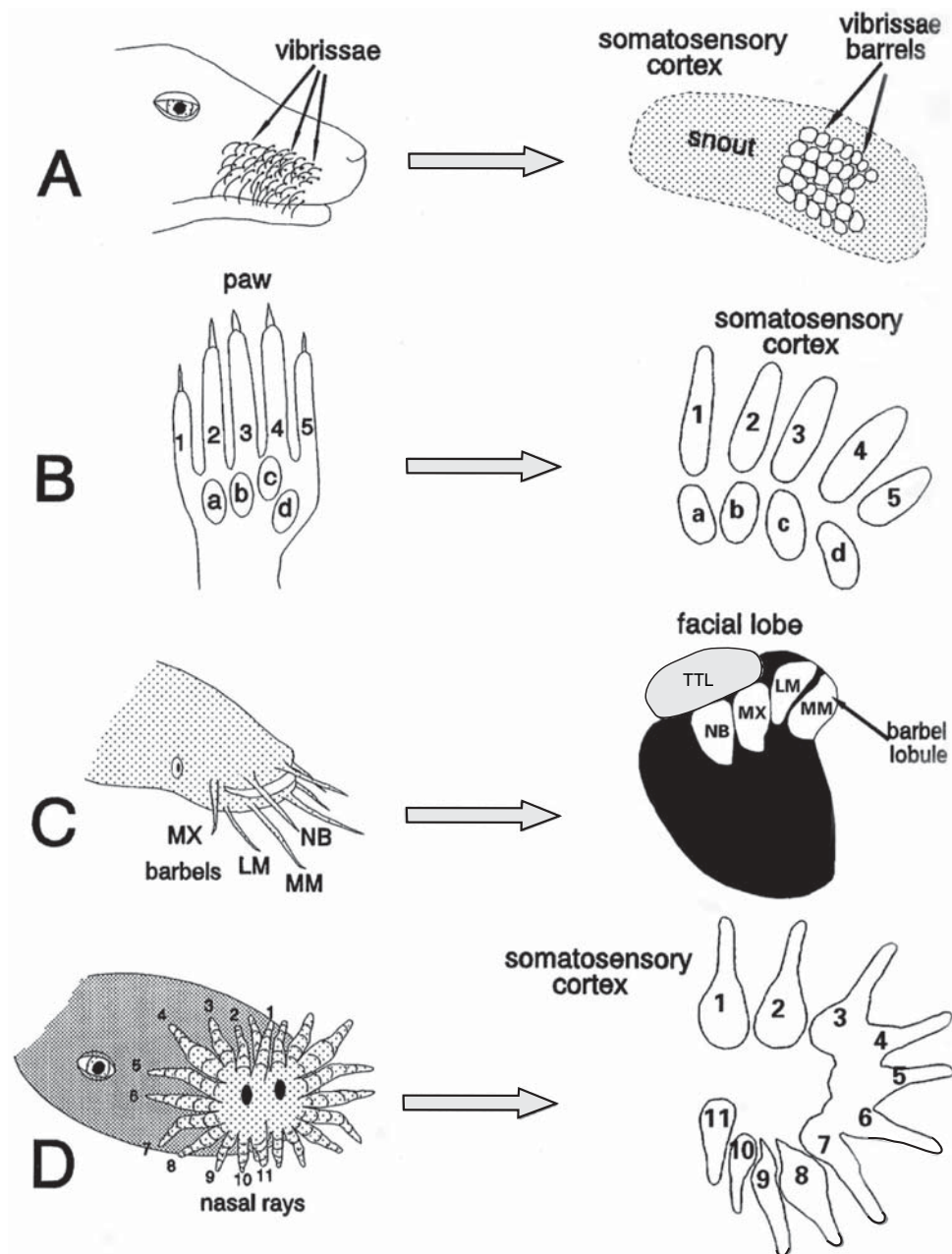


FIGURE 1. Isomorphic representations of peripheral sensory structures within the central nervous system. A: The vibrissae of a rodent and their representation in the somatosensory cortex. B: The ventral surface of the paw of a rodent showing the digits (numbers) and palm pads (letters) and their corresponding somatosensory cortical representation. C: The barbel's gustatory receptors within the animal's facial lobe. The region labeled TTL indicates the representation of the gustatory receptors for the rest of the animal's body. D: The 22 nasal rays on the snout of a star-nosed mole. The 11 nasal rays of the animal's right side shown represented with corresponding numbers on its somatosensory cortex. Adapted from Hodos and Butler (1997).

BOX 2-3. Isomorphic Topographic Maps—cont'd

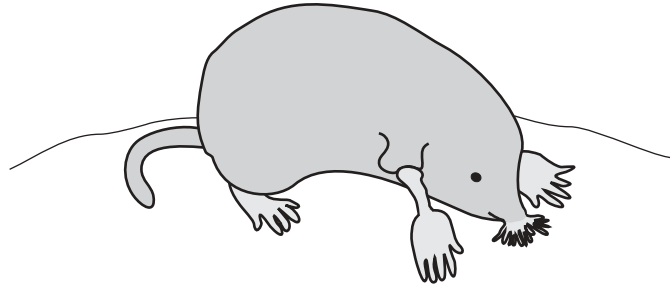


FIGURE 2. A star-nosed mole (*Condylura cristata*).

center of the snout represent the nares. These rays are used to probe the moist earth for earthworms and other prey. Each nasal ray is represented in the animal's somatosensory cortex in an amazing likeness of the peripheral structure's size and location.

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RECEPTIVE FIELDS

In those senses in which either the body surface or the surrounding environment is mapped in a topographic manner, the notion of the **receptive field** has proved quite useful. A receptive field is that area of a sensory surface that must be stimulated in order to influence the activity of a particular sensory neuron in the central nervous system. In the case of vision, the receptive field is that area in visual space in which a stimulus must be presented in order for a neuron in the central visual system to respond. Similarly, a somatosensory receptive field is that region of the body that must be stimulated in order for a central somatosensory neuron to discharge. The existence of discrete receptive fields is the basis of retinotopic and somatotopic organization. The size of the receptive field represents the sum of the excitatory and inhibitory influences present in the sensory pathway that converge on the central sensory neuron. These excitatory and inhibitory influences may be from receptor cells, central sensory neurons, or some combination of both.

THE SENSES AND EVOLUTION OF THE CENTRAL NERVOUS SYSTEM

The diversity of the sensory worlds of animals is matched only by the diversity of the environments that they inhabit. Those animals that achieved the capability to extend their exploration of the sensory world, either by sudden mutation or by more gradual changes in their structure, were able to invade and exploit new adaptive zones to the benefit of themselves and their offspring. These benefits led to further adaptive pressures for increased sensitivity or broader range of responsiveness or altered ranges. In the majority of instances, the development of new sensory adaptations was the wedge that opened the way to new sources of food, new systems for early warning of the approach of predators, more efficient methods for care of the young, better communication with conspecifics, easier detection of the location of potential mates and recognition of their sexual receptivity, and a host of other behavioral adaptations that have promoted both the survival of

existing lineages and the development of new ones. These new sensory adaptations have included increased complexity and organization of topographic maps within the sensory system, the development of multiple topographic maps of the system within the telencephalon, and the emergence of entirely new receptors and/or modification of existing receptors, both of which utilize existing neural pathways. The extreme versatility and adaptability of sensory receptors and their central connections and pathways has been a critical factor in the ability of the central nervous system to evolve and to play a key role in the ability of species to better exploit their present environments or to successfully invade new ones.

INTRODUCTORY NEUROSCIENCE TEXTBOOKS

These books will be useful for readers with little background in cellular neuroscience and other neuroscience topics or for those who need to refresh their knowledge at an introductory level.

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3

The Vertebrate Central Nervous System

INTRODUCTION

One of the principal evolutionary events that preceded the sequences of brain and head evolution in vertebrates was a novel embryological event: the development of the mouth as a distinct body opening that is separate from the original gut opening, at or near which the anus eventually forms. Animals that possess this characteristic are known as **deuterostomes**, which means “second mouth.” Deuterostomes comprise two major groups—the Ambulacraria, which includes echinoderms (starfishes, sea urchins, and many related genera) and hemichordates (pterobranchs and acorn worms), and the Chordata. The extant members of the latter group are the tunicates (sea squirts), cephalochordates (*Branchiostoma*, previously called *Amphioxus*), and vertebrates (hagfishes, lampreys, and jawed vertebrates). Some of the key evolutionary changes in deuterostome and chordate evolution have affected events that occur relatively early in embryological development. Because a basic understanding of embryological development is of great value for understanding brain structure across adult species, we will begin this chapter with a brief overview of this process in vertebrates.

DEVELOPMENT OF THE BRAIN

Following the fertilization of a deuterostome egg, development proceeds with repeated cleavages of the cells (Fig. 3-1). The pattern of cleavage is variable among the different groups of deuterostomes but in all groups results in the formation of a **blastula** [Fig. 3-2(A)], a sphere of cells around a

central cavity, the **blastocoel**. The blastula is already polarized at this stage, with an **animal hemisphere** and a **vegetal hemisphere**. Some differences also exist among deuterostomes in particular features of the course of development following the blastula stage, but a general pattern of development is consistent among all deuterostomes.

In vertebrates, the process of gastrulation (Fig. 3-2) follows the blastula stage, with continued cell proliferation and the specification and arrangement of various groups of cells relative to the parts of the body that they will eventually form. The developing **gastrula** initially consists of two cell layers: an outer layer of cells, the **ectoderm**, which is derived from the animal hemisphere of the blastula and from which the skin and nervous system will form, and an inner layer, which consists initially of **endoderm**. The endoderm is derived from the vegetal hemisphere of the blastula and surrounds the cavity, called the **archenteron**, which will become the lumen of the gut. The archenteron expands during gastrulation, obliterating the blastocoel. The opening of the gut cavity is the **blastopore**. As gastrulation proceeds, the roof of the archenteron, formed by the dorsal part of the inner layer of cells, differentiates to form mesodermal tissue, which in turn gives rise to a midline structure called the **notochord**, as well as to lateral sheets of tissue that will form muscle and bone. The rest of the inner layer remains endoderm, the tissue of the gut.

During the later stages of gastrulation, the notochord and the part of the mesoderm immediately rostral to it, called the prechordal mesoderm, induce formation of the neural tube. In the absence of signals from the mesoderm, the ectoderm is prevented from achieving a neural fate by the action of **bone morphogenetic proteins (BMPs)**. The dorsal mesoderm, including the notochord, releases several molecules, such as

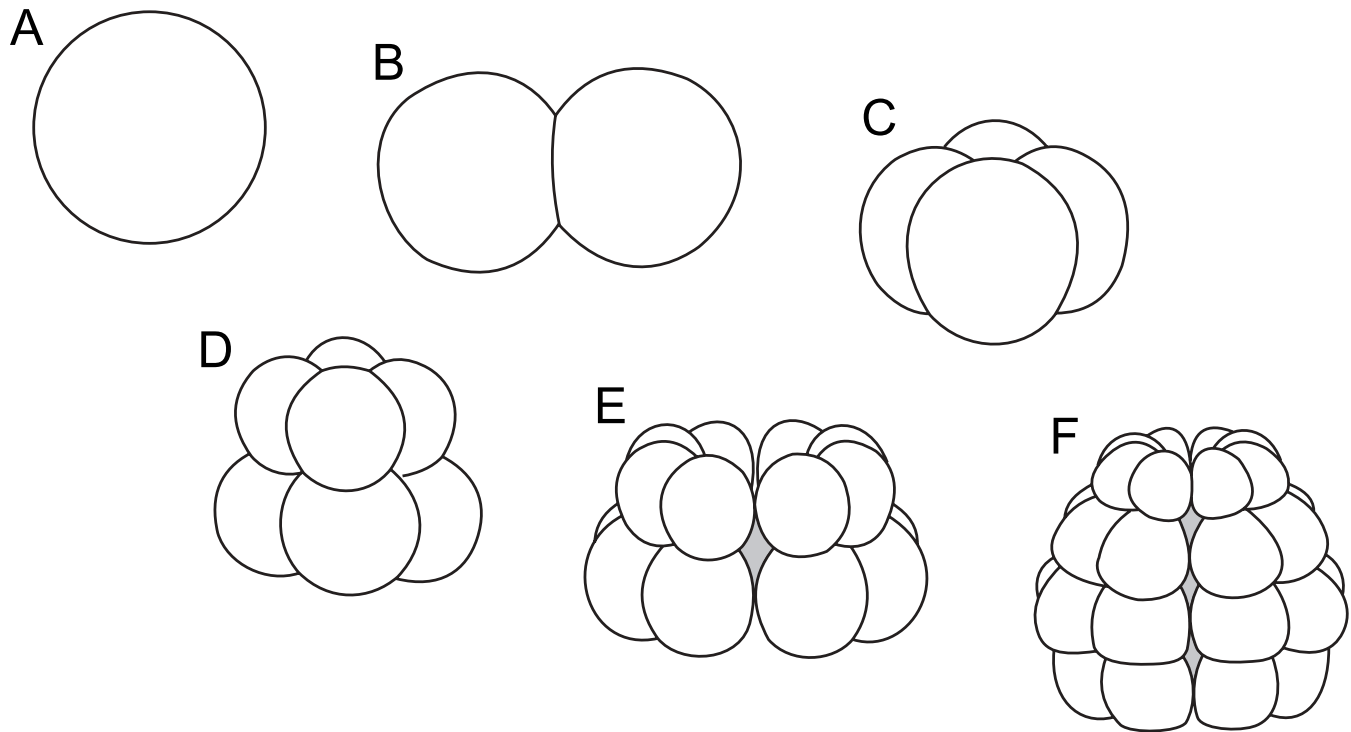


FIGURE 3-1. Earliest stages of cell division beginning with a single-celled, fertilized egg (A) with subsequent divisions up to the 32-cell stage (F), which with continued cell division will eventually form the blastula. After Liem et al. (2001). Used with permission of Thomson Learning Global Rights Group.

the proteins **chordin**, noggin, and ceberus. These molecules block the action of the BMPs in the overlying ectoderm, allowing it to thicken and form the **neural plate** [Fig. 3-2(E,F)]. A pair of **neural folds** [Fig. 3-2(F)] develops along this plate; the folds grow dorsally, meet and then fuse to form the **neural tube** (Fig. 3-3). The lumen (inner space) of this tube forms the ventricular system, while the central nervous system, composed of the brain and spinal cord, develops within the walls of the tube.

Segmental Development of the Vertebrate Brain

The vertebrate brain comprises three main divisions, which, from rostral to caudal, are the **prosencephalon** ("forward brain"), **mesencephalon** ("middle brain"), and **rhombencephalon** ("rhomb" referring to the rhomboid shape of its ventricle). The prosencephalon, or **forebrain**, has two parts: the **telencephalon** ("end brain") and the **diencephalon** ("through brain"). The mesencephalon, or **midbrain**, is a single entity, and the rhombencephalon, or **hindbrain**, has two parts: the **metencephalon** ("after brain"), which comprises the cerebellum and the rostral part of the hindbrain, and the **myelencephalon** ("marrow brain," referring to its continuity with the spinal cord), which is the more caudal part of the hindbrain.

During embryological development, the neural tube undergoes a series of flexures in the rostrocaudal direction. The

rostral part of the brain flexes ventrally [Fig. 3-4(A)]. A transverse, ventral fold develops on the ventral surface of the tube in the position where the pituitary gland will form. A pair of lateral bulges in the rostral part of the forebrain forms the cerebral hemispheres of the telencephalon. A single eye stalk initially emerges from the rostral-most aspect of the hypothalamus, which is the most ventral division of the diencephalon. Under the influence of the signaling molecule **Sonic hedgehog (Shh)**, which is released from the more ventrally lying mesoderm, the eyestalk splits in two to form the paired eyes. The epithalamus, which is the most dorsal division of the diencephalon and which includes the epiphysis [Fig. 3-4(B)], develops in the dorsal part of the diencephalon.

The midbrain lies caudal to the ventral fold in the neural tube. Paired bulges in the roof of the midbrain expand to form the **tecta** (plural of **tectum**), or roof of the midbrain, while the more ventral part of the midbrain becomes the **tegmentum** (the main body of the midbrain). The dorsal portions of both the caudal midbrain and the rostral hindbrain enlarge to form the cerebellum [Fig. 3-4(B)].

The central nervous system, despite the complexity of its structural components, is basically a hollow tube, the lumen of which is the central canal and the brain ventricles. During embryonic development, the neural tube is formed by the folding of the neural plate, as discussed above. In the rostral part of the neural tube, which will eventually become the brain, a rostrocaudal series of bulges, called **neuromeres**, then develops. The neuromeres, which are serial brain segments,

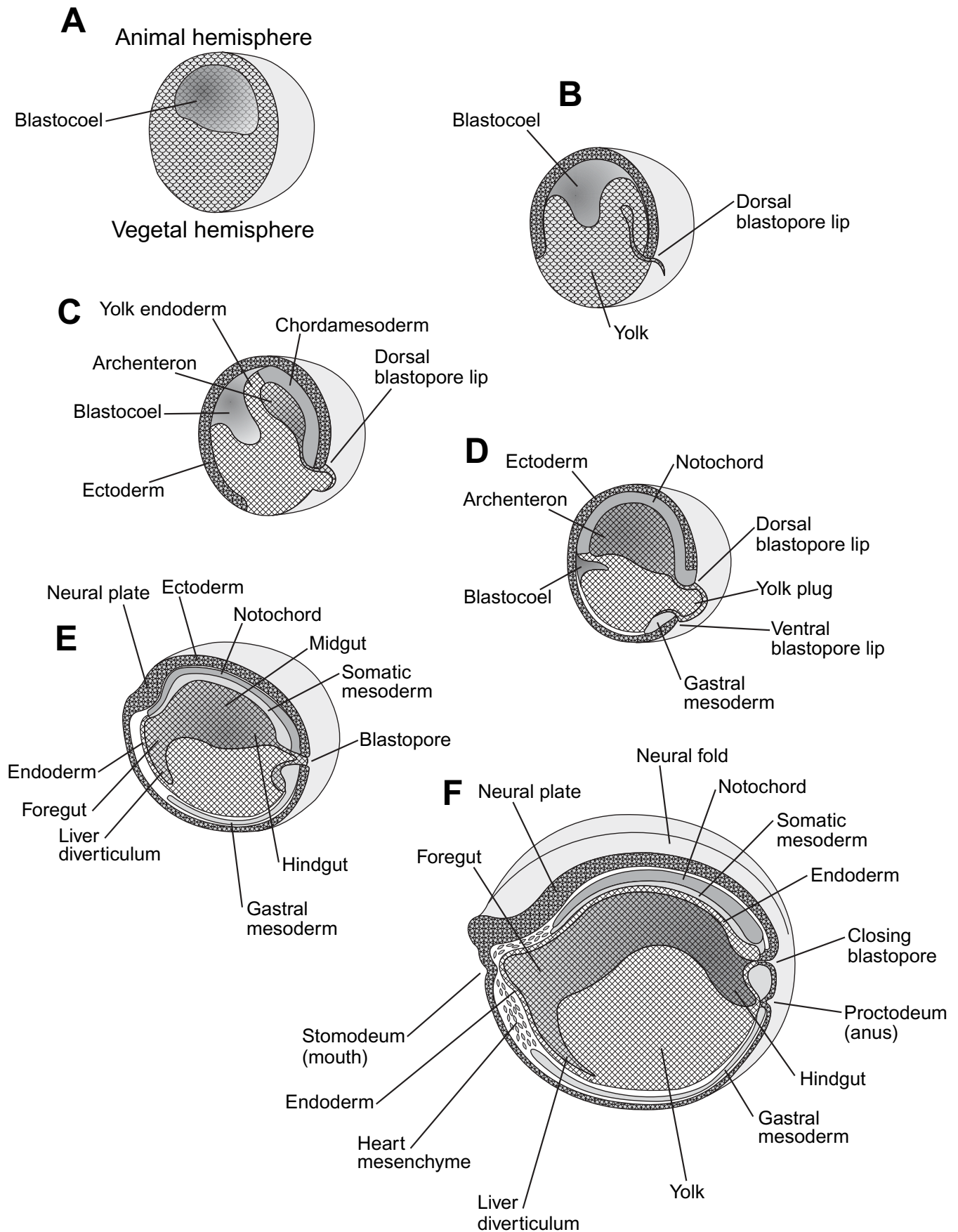


FIGURE 3-2. Drawings of sections through a blastula (A) and stages of gastrulation (B–F) to form an embryo in a frog. In B–F, rostral is toward the left. A–E are sagittal sections viewed from a slight angle, whereas F is drawn in the true sagittal plane. Modified from drawings in Rugh (1964), which were adapted from a 1949 publication by Huettnner, with additional information from Liem et al. (2001) and Gilbert (1994). Used with permission of Elizabeth Rugh Downs.

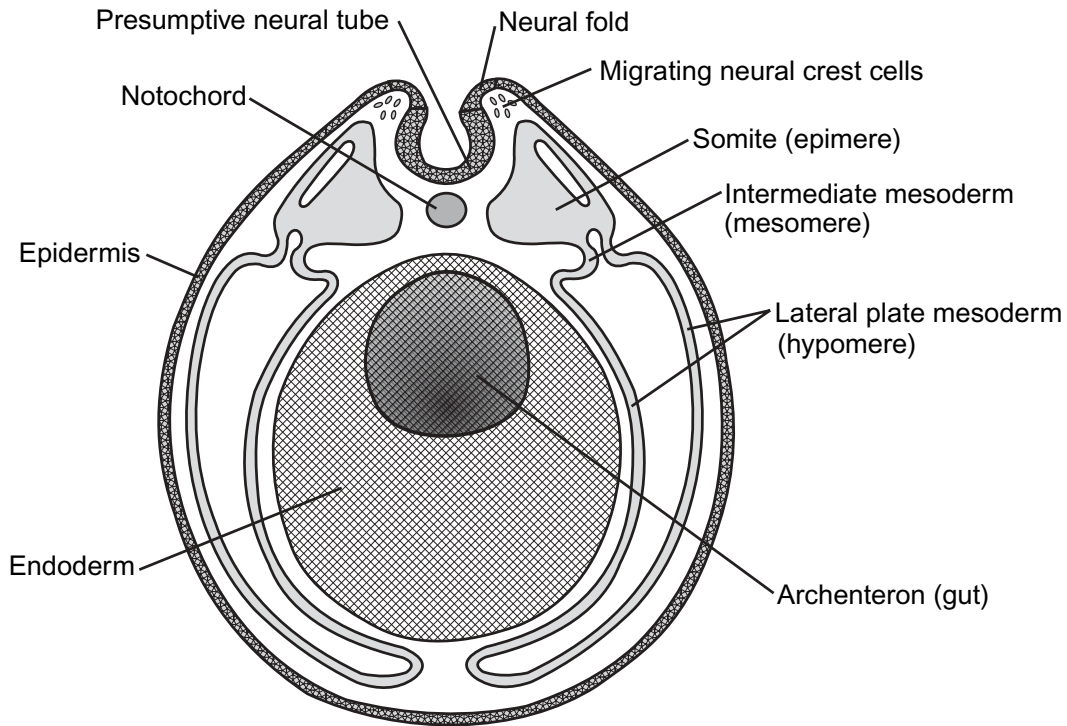


FIGURE 3-3. Transverse section through the body of a generalized vertebrate at about the same stage as that shown in Fig. 3-2(F). The endoderm now completely encircles the archenteron. The mesoderm consists of epimere, mesomere, and hypomere. The neural tube is in the process of closing over and will then separate from the overlying ectoderm. After Liem et al. (2001). Used with permission of Thomson Learning Global Rights Group.

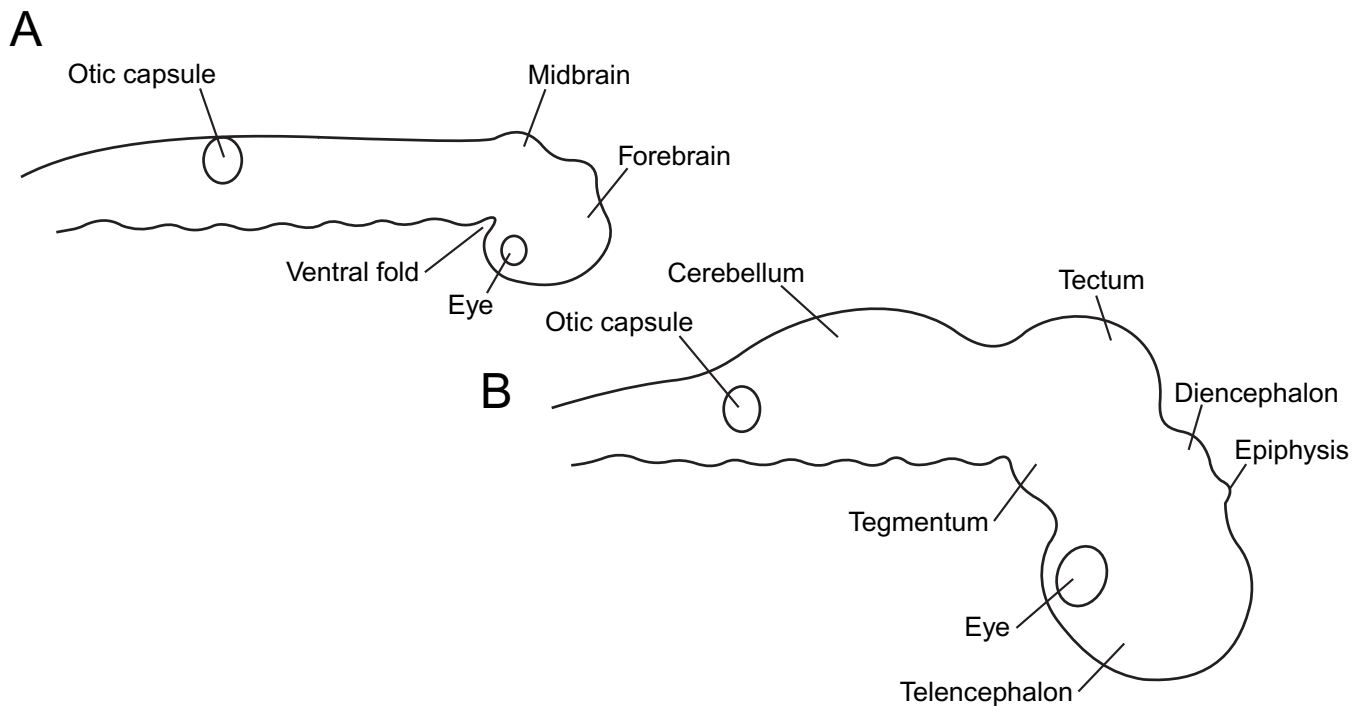


FIGURE 3-4. Diagram of the flexure of the neural tube during formation of the brain. Rostral is toward the right.

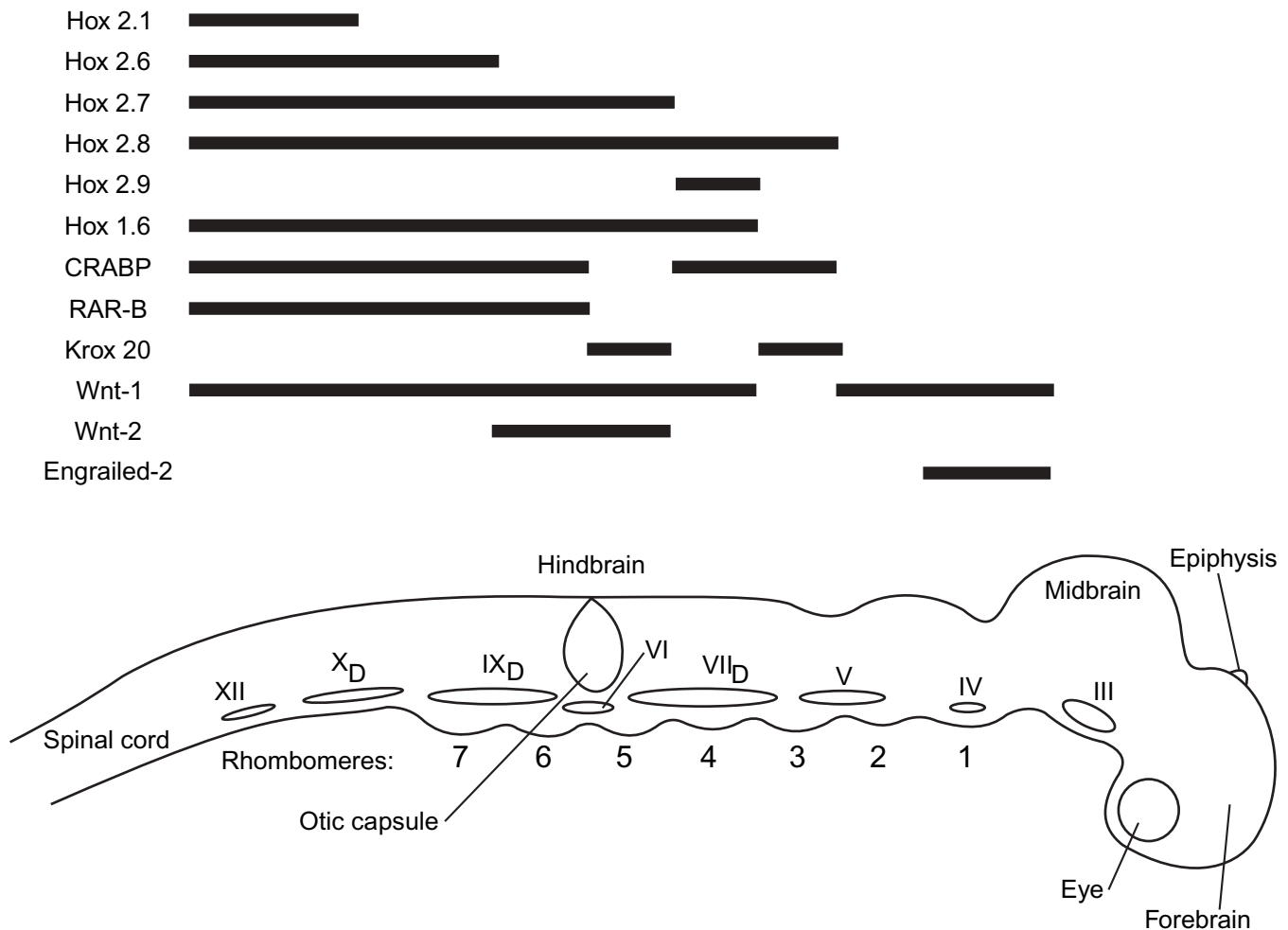


FIGURE 3-5. Schematic sagittal section through the developing chick brain, showing the expression patterns (indicated by the bars) of homeobox-containing and similar regulatory genes in the hindbrain and midbrain and the location of the populations of neurons for a number of the cranial nerve motor nuclei. The latter are indicated by Roman numerals, consistent with the terminology and classification of cranial nerves discussed in later chapters. Rhombomeres are indicated by Arabic numbers 1–7. Rostral is toward the right. Adapted from Noden (1991). Used with permission of S. Karger AG, Basel.

were identified in the early 1900s and formed the basis of a **neuromeric theory**. This theory postulated that the neuromeres are specified by genetic fate determinants and constitute longitudinal and transverse segmental divisions, or compartments, of the neural tube that have independent and individual developmental fates.

In the hindbrain (rhombencephalon), the neuromeres are called **rhombomeres** (Fig. 3-5); at least seven rhombomeres are present, and they are delineated by a series of transverse grooves on the external and internal surfaces of the neural tube. In the midbrain (mesencephalon) and forebrain (prosencephalon), a series of transverse grooves is not readily apparent, but segmental divisions are present there as well (Fig. 3-6). These divisions in the midbrain are called **mesomeres** and those in the forebrain **prosomeres**. To date, six prosomeres (p1–p6) and two mesomeres (m1 and m2) have been recognized. It should be noted that whereas the rhombomeric boundaries are barriers to neuronal migration across them

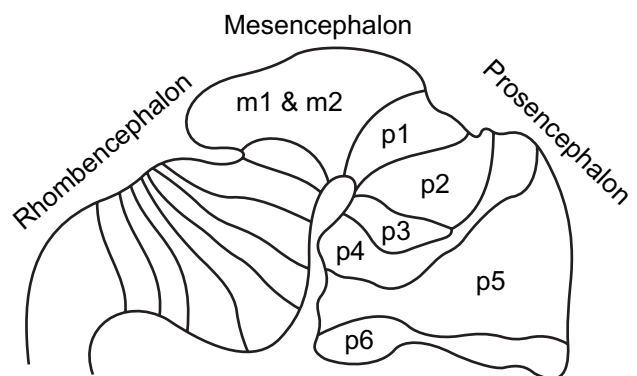


FIGURE 3-6. Drawing of a schematic lateral view of the developing brain of a chick embryo with the segmental neuromeric divisions projected onto it. The prosomeres are identified as p1–p6 and the two mesomeres as m1 and m2. Rostral is toward the right. Adapted from Puellas and Rubenstein (1993). Used with permission of Elsevier.

during the neuronal proliferative period, the prosomere boundaries within the forebrain are not. Thus, the latter should not in fact be accorded the “meric” designation. Because this terminology has been used in the literature, however, and has not yet been replaced with other terminology, we have used it here.

The individual segmental specification of the rhombomeres has recently been correlated with the expression patterns of certain regulatory genes (Fig. 3-5). These regulatory genes are involved in specifying rostrocaudal axial patterning in the developing embryo. Over the past decade, a new area of research on such regulatory genes has blossomed. These genes are referred to as **homeobox-containing genes** because they contain a specific sequence of DNA nucleotide base pairs called the **homeobox**. Homeobox sequences are widely distributed in vertebrate genes and are homologues of genes identified in the fruit fly *Drosophila* and various other invertebrates. Homeobox genes control segmental development by their role as DNA-binding transcriptional regulators, thus affecting the expression of a number of other genes involved in the developmental process. The first subfamily of homeobox genes to be identified were called **Hox genes**. Various other subfamilies of these regulatory genes have other conserved sequences in addition to the homeobox, such as the “zinc-finger” gene (*Krox-20*) and **paired box (Pax)** genes, and are also involved in the pattern specification of the brain. The names of these genes often reflect particular traits that occur with mutation of the gene, as with the “zinc-finger” gene.

A different and unique combination of homeobox-containing genes is expressed in each of the rhombomeres. In the top part of Figure 3-5, the extent of each black bar indicates the part of the brainstem in which activity for the particular gene listed at the left has been detected. For example, the *Hox 2.8* gene is active in a long area extending from the 2-3 rhombomere boundary caudally through the caudal-most part of the brainstem, whereas the *Krox-20* gene has two discrete areas of activity, one in rhombomere 3 and the other in rhombomere 5. The total pattern of gene activity thus forms a bar code or fingerprint-like profile that is unique for each individual rhombomere.

Whether the combined activity of these genes determines the specific identity of each rhombomere, the cranial nerve nuclei within the rhombomere, or both has not yet been established, however. During embryological development, following the main stage of neuronal proliferation, the neuron cell bodies that form the motor nuclei of cranial nerves migrate caudally within the neural tube to reach their final rhombomeric positions. Motor neurons of the seventh, ninth, and tenth cranial nerves and some of the neurons of the fifth and lateral line cranial nerves migrate over distances of one to three rhombomeres. How the activity of the regulatory genes specifies the various pools of motor nerve neurons in relation to the rhombomeric segments is thus unclear.

In the midbrain and forebrain, a number of similar homeobox-containing genes specify the mesomeres and prosomeres. These include genes referred to as the *engrailed* homologue, *En-2*, as well as *Krox-20* in the midbrain and as *Wnt-1*, *Wnt-3*, *Wnt-3A*, *Wnt-4*, *Dix-1*, *Dix-2*, *Nkx-2.2*, and so on, in the forebrain. Many of the same genes also specify brain development in invertebrates, such as *Drosophila*.

Neurogenesis and Migration of Neurons

As the neural tube differentiates rostrocaudally, it also differentiates into dorsal and ventral regions due to the actions of other regulatory genes. After closure of the neural tube [Fig. 3-7(A,B)], the underlying notochord produces the signaling factor Sonic hedgehog [Fig. 3-7(C)], which induces the differentiation of a specific group of cells in the ventral midline of the neural plate, called the **floor plate**. These cells then also produce Sonic hedgehog, which promotes a ventral fate for the ventral part of the neural tube. This ventral half of the neural tube becomes the **basal plate**, which contains motor neurons. Other signaling molecules—bone morphogenic proteins (BMPs)—arise from the ectoderm dorsally and later from the **roof plate**, which comprises cells in the dorsal part of the neural tube itself. BMPs antagonize Sonic hedgehog and promote a dorsal fate. Under their influence, the dorsal part of the neural tube becomes the **alar plate**, which is sensory in nature. Even though BMPs can suppress any neural fate for the ectoderm of the gastrula, as discussed above, they also can act here, in lower concentrations, to promote alar plate formation.

Outside the neural tube, in the presence of slightly higher levels of BMPs, additional populations of neurogenic cells give rise to the neurons of the peripheral nervous system. In the body and the head, cells that initially lie between the neural tube and the surface ectoderm, the **neural crest** [Figs. 3-3 and 3-7(A,B)], contribute to many diverse tissues, including the flat bones of the skull, the so-called visceral arches of the jaw, hyoid and gill/throat regions, cells of the adrenal medulla, and melanocytes, and also give rise to sensory and motor neuron cell bodies of the peripheral nervous system. In the head, specific areas of ectoderm, called **neurogenic placodes**, lie lateral to the neural crest and also contribute neurons to the sensory ganglia of cranial nerves. The neural derivatives of both neural crest and neurogenic placodes are considered in detail in the later chapters that cover the cranial nerves.

Within the neural tube, the central nervous system is formed by a complex process that begins with the genesis of glial cells and neurons [Fig. 3-7(D)]. Cell proliferation occurs primarily within the **ventricular zone**, which encircles the ventricular lumen. Astrocytes are produced from the earliest stages. These astrocytes are called **radial glia**, since they assume an elongated shape and span the width of the tube in a radial array from the **luminal surface** of the ventricle to the **abluminal surface** at the peripheral surface of the neural tube. As neuron cell bodies are produced, they migrate away from the region of the lumen along the shafts of the radial glia. In fact, the developing neurons produce a morphogen that maintains the radial shape of these glial cells. After neurogenesis ceases, the astrocytes can then assume the star shape for which they are named.

The degree of luminal-abluminal, or radial, migration differs markedly among different vertebrates and in different regions of the brain. The pattern of migration also varies, with nuclei and cortices being formed in different ways. In this section, we will briefly examine some of the various ways in which the neurons are assembled into structures within different regions of the brain and among different groups of vertebrates. The developmental processes involved in producing

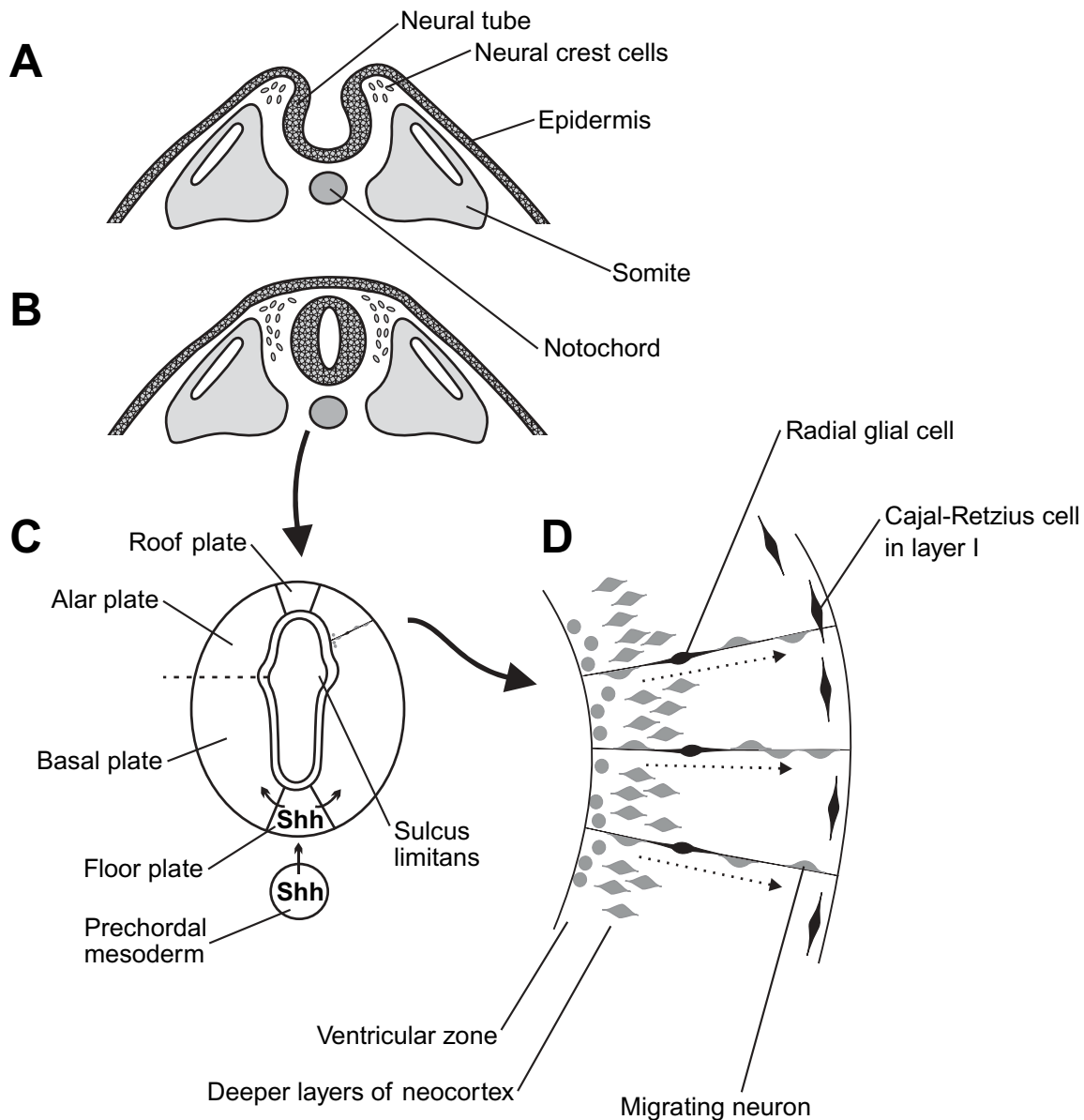


FIGURE 3-7. Drawings of the upper part of transverse sections through the developing vertebrate body (A and B), as can be compared with Fig. 3-3, to show the position of the closed neural tube (B), notochord, and neural crest cells. C: Drawing of a transverse section through the developing brain as it receives the Shh signal from the underlying prechordal mesoderm and, in turn, its own floor plate. A single radial glial cell and migrating neurons are shown in the right alar plate. The latter process is drawn in D at a higher magnification and for the special case of mammalian neocortex, with generated neurons migrating along the radial glial cells. Note that, in D, several layers that lie between the ventricular zone and the deeper layers of neocortex are omitted. The details of this region, including these layers, are shown in Fig. 3-8.

the individual neurons and their connections are complex and also subject to disruption by both local factors and more external influences. The timing of sequences in multiple groups of neurons must be properly phased for normal development to occur. The production and migration of populations of neurons to form nuclei and cortices also occurs in specifically timed sequences, since targets must be established for the growing, incoming axons to locate and reach.

Cortices and Nuclei

As discussed in Chapter 2, two basic structural patterns for populations of neurons are **cortices**, which are laminated structures that tend to be located in the more dorsal, alar plate parts of the brain, and **nuclei**, which are prevalent in both the alar and basal plates. Nuclei may consist of diffusely scattered, either loosely or more tightly packed cells or of cells aligned

in a laminar pattern, reminiscent in some cases of cortex. A number of cortical areas is present in the rostral part of the brain in some vertebrates, and cortex is also present in the roof of the middle part of the brain (midbrain) and of the hindbrain.

Cortical areas such as the neocortex in mammals and the optic tectum in many vertebrates are formed by serial migrations of generated neurons. Neocortex is an extensive region of generally six-layered cortex that forms the largest part of the pallium, the upper (dorsal) portion of the telencephalon. The neurons of neocortex arise from two different sources, one of which is the local ventricular zone of the pallium and the other of which is located external to the cortex in the subpallium, the lower portion of the telencephalon. The first step in the process is the formation of the **marginal zone**, which eventually becomes the outermost cortical layer, layer I. It is populated by **Cajal-Retzius cells** [Figs. 3-7(D) and 3-8], which are generated within the pallium. At this stage, these cells together

with early-generated neuronal precursors form a single structure, called the **preplate**. Subsequently, generated neurons from the ventricular zone pass through the **subventricular** and **intermediate zones** (Fig. 3-8) and split the preplate into the definitive marginal zone and the lower layer of the preplate, which is now called the **subplate**. The **cortical plate**, in which layers VI–II of neocortex form, thus comes to lie between the marginal zone and the subplate. The subplate becomes incorporated into layer VI as its deep portion.

The neurons that arise in the ventricular zone and migrate radially into the cortical plate become the excitatory, glutamatergic components of the cortex. Within the cortical plate, the deeper-lying neurons are produced before the more superficially lying ones. This pattern of migration is called “**inside-out**” and is the result of the action of **reelin**, which is a patterning molecule that is produced by the Cajal-Retzius cells in the marginal zone, and other patterning molecules. Reelin

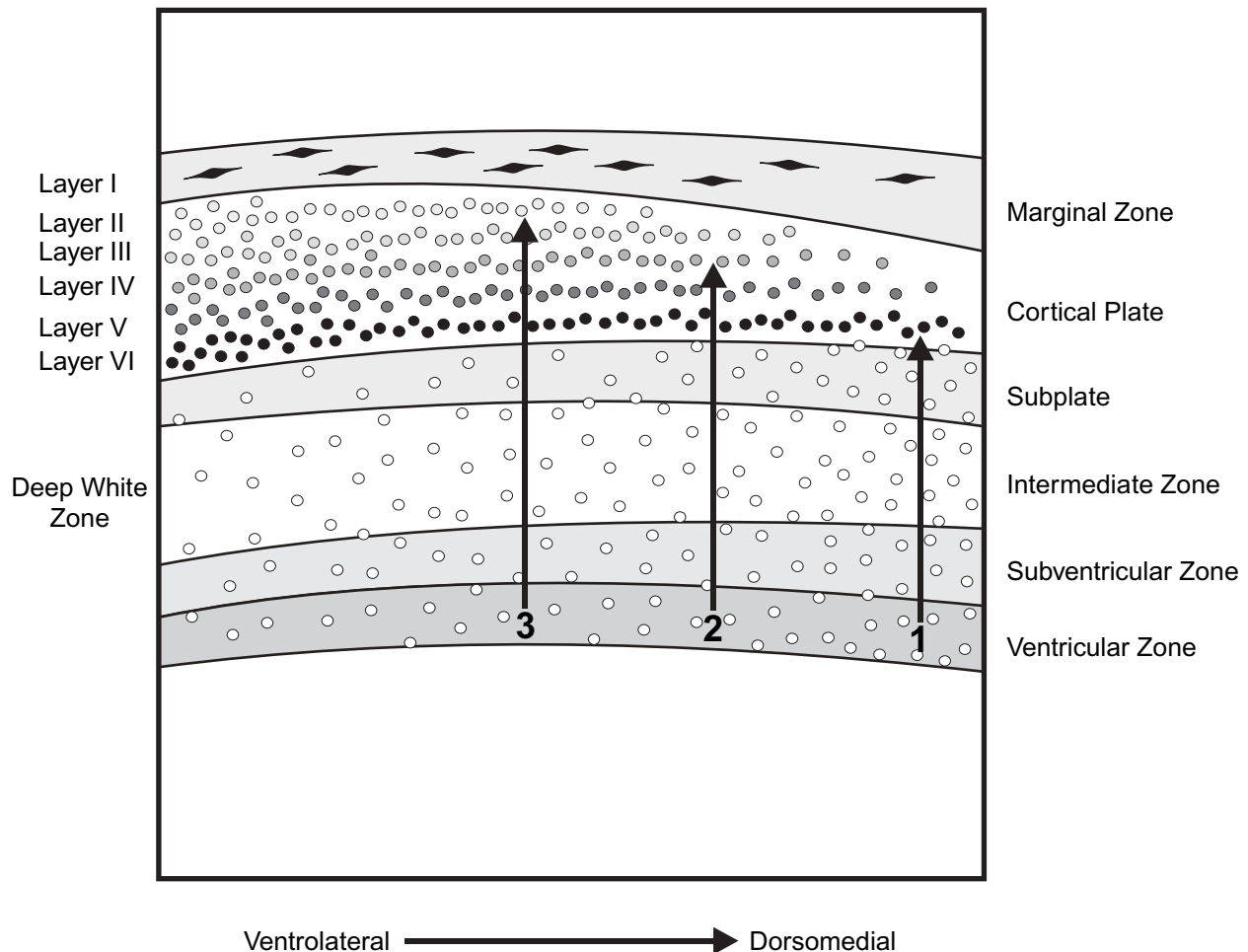


FIGURE 3-8 Drawing showing the progressive formation of neocortical layers VI–II within the cortical plate, with the neurons that form the deepest layer, layer VI, being generated earliest (arrow 1), those in the intermediate layers V–III generated subsequently and in deep to superficial order (arrow 2), and the most superficial layer, layer II, generated last (arrow 3). Cajal-Retzius cells are shown in the marginal zone, which becomes layer I. Neurons migrating radially into the cortical plate stop when they encounter the reelin signal produced by the Cajal-Retzius cells. The drawing reflects the ventrolateral (left) to dorsomedial (right) gradient of maturation of the neocortex.

inhibits the migration of the newly produced neurons. Thus, as those that will form layer VI pass through the subplate, they encounter the reelin signal and stop migrating. The layer V neurons subsequently pass through the subplate and the layer VI neurons, then encounter the reelin signal, and stop migrating. Layers IV–II are formed in a like manner. As corticogenesis comes to an end, most of the cells in layer I die off and disappear, resulting in its being an almost cell-free zone.

In addition to the neurons that arise from the ventricular zone and migrate radially to form the five main cellular layers of the neocortex, other neurons arise from the subpallium. The subpallium produces several populations of precursor neurons that migrate tangentially into the cortical plate and become the GABAergic, inhibitory neurons of the cortex. Some of these neurons migrate for substantial distances to reach the more dorsomedial cortical regions. Unlike the radial migration of the glutamatergic neurons along radial glial cells, the mechanics of tangential migration are obscure.

As the layers of the cortical plate are formed, the growth of axons and dendrites is initiated, and connections, both distant and local, are established. The nuclei of the dorsal thalamus (that lies within the diencephalon) have extensive and for the most part reciprocal connections with the neocortex. The subplate neurons, some of which contribute to the deeper part of layer VI, are the first to give rise to axons that extend toward the dorsal thalamus. They meet the ascending thalamocortical axons part of the way along, and the two sets of fibers interdigitate. The meeting and interdigitation being essential for the eventual completion of these pathways has been called the **handshake hypothesis**. The ascending and descending fibers use each other as guides, much as if you slid your right hand along your left wrist and up your left sleeve, and vice versa.

The distal end of each in-growing afferent axon is a specialized structure called a **growth cone**, which is the site of elongation of the axon. As the thalamocortical fibers from the various dorsal thalamic nuclei reach the pallium, they use cues from the subplate neurons to recognize their correct locus of termination. The axons arrive before their main target cell layer (layer IV) has been generated, but they wait for these target cells to be formed and do not grow beyond that area. However, if the subplate cells are selectively destroyed, the arriving dorsal thalamic axons do not halt in the proper position but continue growing beyond their normal area of termination and on into adjacent, unrelated areas of cortex. The subplate cells thus seem to provide a necessary signpost for the growth cones of the afferent dorsal thalamic axons.

There is a high degree of specificity in the connections of cortical structures, made possible by their geometric configuration. Different afferent axons terminate on different, specified parts—superficial to deep—of the dendritic trees of the cortical neurons. The entire area of a given cortical region is also frequently in receipt of specifically ordered projections, so that the point-to-point mapping of sensory or motor space from the external world of the animal is mapped in order onto the cortex. In-growing axons may sometimes form connections in the wrong location with reference to the map, but these axons later retract and then form connections in the place that is congruent with the map of external space. These adjustments occur as sensory information comes over the afferent axons and into the cortex.

The nuclei in the brain, as well as some of the cortices, are formed by cellular migrations along radial glia that mostly proceed in an “**outside-in**” pattern, the opposite of that in the neocortex. In this case, the more superficial, lateral groups of neurons are generated first. There are additional spatiotemporal gradients that have been identified in the dorsal thalamus. Caudal nuclei develop earlier than more rostral ones, and ventral nuclei develop earlier than more dorsal ones. Thus, different areas of the periventricular matrix give rise to different sets of nuclei at different times.

While nuclei form by different migration patterns than those of neocortex, a number of nuclei have point-to-point maps that correspond to those found in neocortex. The nuclei that have such maps are generally those that project to or have reciprocal connections with cortical, mapped areas. In mammals, for example, the **dorsal lateral geniculate nucleus**, the dorsal thalamic nucleus that is reciprocally connected with primary visual cortex, has a point-to-point map of visual space in each of its multiple, separate layers of cells. A similar map is present in a midbrain nucleus of many vertebrates, **nucleus isthmi**, which has reciprocal, point-to-point connections with the **optic tectum**, the visual part of the midbrain roof. Maps are also established and maintained in other ascending sensory systems, including the auditory and lateral line systems and the somatosensory system. Axonal connections throughout the brain depend on a variety of guidance mechanisms to form correctly. As in the case of neocortex discussed above, the growth cone at the tip of the elongating axon is a crucial site for these processes.

As nuclei are formed by migrations of cells, some regions of the periventricular matrix may give rise to one or more specific nuclei. Such a region is called a **developmental field** (as discussed in Box 1-1 in Chapter 1). The number of distinct nuclei that arise from a given field may be different in different groups of vertebrates. Also, all the cells or cell groups produced by a field during development may not be retained in the adult if the proper connections are not made at the proper time. Such occurrences would affect the phenotype and may play a role in evolutionary change. A subtle alteration in timing or in the presence or absence of local molecular cues, produced by a mutation in the genome, could result in the lack of a particular cell group in the adult and/or the appearance of a “new” cell group with new connections. The concept of field homology applies to such situations and was discussed in Chapter 1.

Differing Patterns of Development

Within each of the major groups of vertebrates, one marked difference in brain development is present that will be discussed in detail in Chapter 4—that of wide variation in the degree of radial migration of neurons, both cortical and nuclear, away from the periventricular matrix. Those vertebrates in which relatively limited migration occurs, that we have designated as Group I, include some species from each of the four major vertebrate radiations: lampreys, some cartilaginous fishes, some ray-finned fishes, and some sarcopterygians (fleshy lobed-finned fishes and their tetrapod descendants). In contrast, hagfishes and other species in each of the three radiations of jawed vertebrates (Group II) have much more extensive migration of neurons and the formation of multiple,

BOX 3-1. What Is “Neo” About Neocortex, and What Is “Iso” About Isocortex?

The large portion of the cerebral cortex of mammals that generally exhibits six cell-and-fiber layers is variously referred to as “neocortex” or “isocortex.” Neither term has the cachet of being entirely satisfactory. The former term originally was proposed in the mistaken belief that this cortex is evolutionary new, i.e. more recently evolved, than the remaining parts of the cerebral cortex, the “archicortex” (hippocampal pallium) and the “paleocortex” (olfactory cortices). The prefixes “archi” and “paleo” both mean old. These parts of the cerebral cortex generally exhibit three layers but include the so-called transitional cortices that have four to five layers.

The term “isocortex” subsequently was proposed as an alternative term to neocortex. “Iso” means “the same” or “equal.” The complementary term “allocortex,” meaning “different cortex,” refers to the olfactory and hippocampal cortical regions, including the transitional cortices. The term isocortex has not been universally adopted and is not an accurate descriptor, however. As a global term, it grammatically begs for a comparison: the same as what? As an intraregional term, it is incorrect. All of the cortical areas that it refers to are not uniformly composed of six cell-and-fiber layers. For example, some regions are called agranular cortex because they lack the granule cells that comprise layer IV in other regions. Additionally, marked differences in

cytoarchitecture (cell architecture, sometimes called cytoarchitectonics) and in myeloarchitecture (fiber architecture) occur across different regions. The German neuroanatomist Korbinian Brodmann based his identification, published in the first decade of the 20th century and now widely used, of dozens of different areas on these differences. These very differences also argue against the use of Brodmann’s own alternative term, “homogenetic cortex,” for neocortex, which has never enjoyed wide acceptance.

In the sense of being evolutionarily more recent than archicortex or paleocortex, we agree that neocortex is not an accurate term. On the other hand, in terms of generally having six layers, this region of the pallium is uniquely mammalian and was a new innovation that occurred at or about the origin of mammals. In this sense of being a novel feature of mammalian brains, the term neocortex is legitimate. Also, with the declining use of the terms paleocortex and archicortex, the relative age of these cortices is a less salient issue. We used the term “isocortex” in the first edition of this book, but, for the reasons discussed here, we have decided to use “neocortex” in this second edition. It strikes us as highly ironic that a fully satisfactory, phylogenetically neutral, and accurately descriptive term for the hallmark of the mammalian brain remains elusive.

distinct layers in cortical structures as well as a greater number of discretely recognizable and larger nuclei. Two other major differences in the development of the brain among different vertebrates will be considered in this chapter. These developmental differences result in marked differences in the organization of the telencephalon.

In the initial phase of development from the closed neural tube, the telencephalon develops by a process called **evagination** in most vertebrates, including lampreys, cartilaginous fishes, amphibians, and amniotes. The central lumen of the neural tube enlarges to form the telencephalic ventricles as the telencephalon bulges outward and expands, that is, evaginates. This process is shown in Figure 3-9(A). After evagination, the part of the pallium that was originally in the most dorsomedial position (A) around the central lumen comes to lie in the most medial part of the telencephalon. This pallial area forms the hippocampal formation (the functions of which include memory and emotion) in the adult. The originally intermediate pallial area (B) becomes the dorsal pallium, which forms part or all of the major sensory, integrative, and motor pallial areas in the adult. The originally ventrolaterally-lying pallial area (C) comes to lie most laterally and gives rise to the olfactory, or lateral, pallium. A fourth pallial area, the ventral pallium, has recently been recognized in amniotes. It has been combined with the lateral pallial region in Figure 3-9 for simplicity.

In contrast, a different process takes place in the development of the telencephalon in ray-finned fishes. The areas in

the basal part of the telencephalon are similarly aligned in all vertebrates, but the pallium undergoes a process called **eversion**. The part of the roof of the neural tube over the central lumen thins and elongates, and the pallial parts of the hemispheres bend outward [Fig. 3-9(B)]. After eversion, the originally most dorsomedial part of the pallium (A) comes to lie in the most lateral, or distal, position in the telencephalon. The originally intermediate part of the pallium (B) lies most dorsally, as in other vertebrates. The originally most ventrolateral pallial area (C) comes to lie in the most medial, or proximal, position in the telencephalon of the adult. Thus, in comparison with other vertebrates, the mediolateral positions of the hippocampal (A) and olfactory (C) pallial areas are reversed in the ray-finned fishes. The process of eversion reverses the topography of the pallial areas (A-B-C-D to D-C-B-A) but preserves the ordinal sequence of the regions—the topology (A-B-C-D or D-C-B-A as opposed to a disarranged sequence such as C-D-B-A). As discussed in subsequent chapters (see Chapter 25), whether this topographical reversal with preservation of topology actually occurs in the pallium of all or even some ray-finned fishes remains a matter of continuing investigation and debate.

A second major difference in telencephalic development occurs between the mammals on one hand and the nonmammalian amniotes on the other. In both mammals and sauropsids (reptiles and birds), the pallium evaginates as diagrammed in Figure 3-9(A). However, how various regions of the pallium

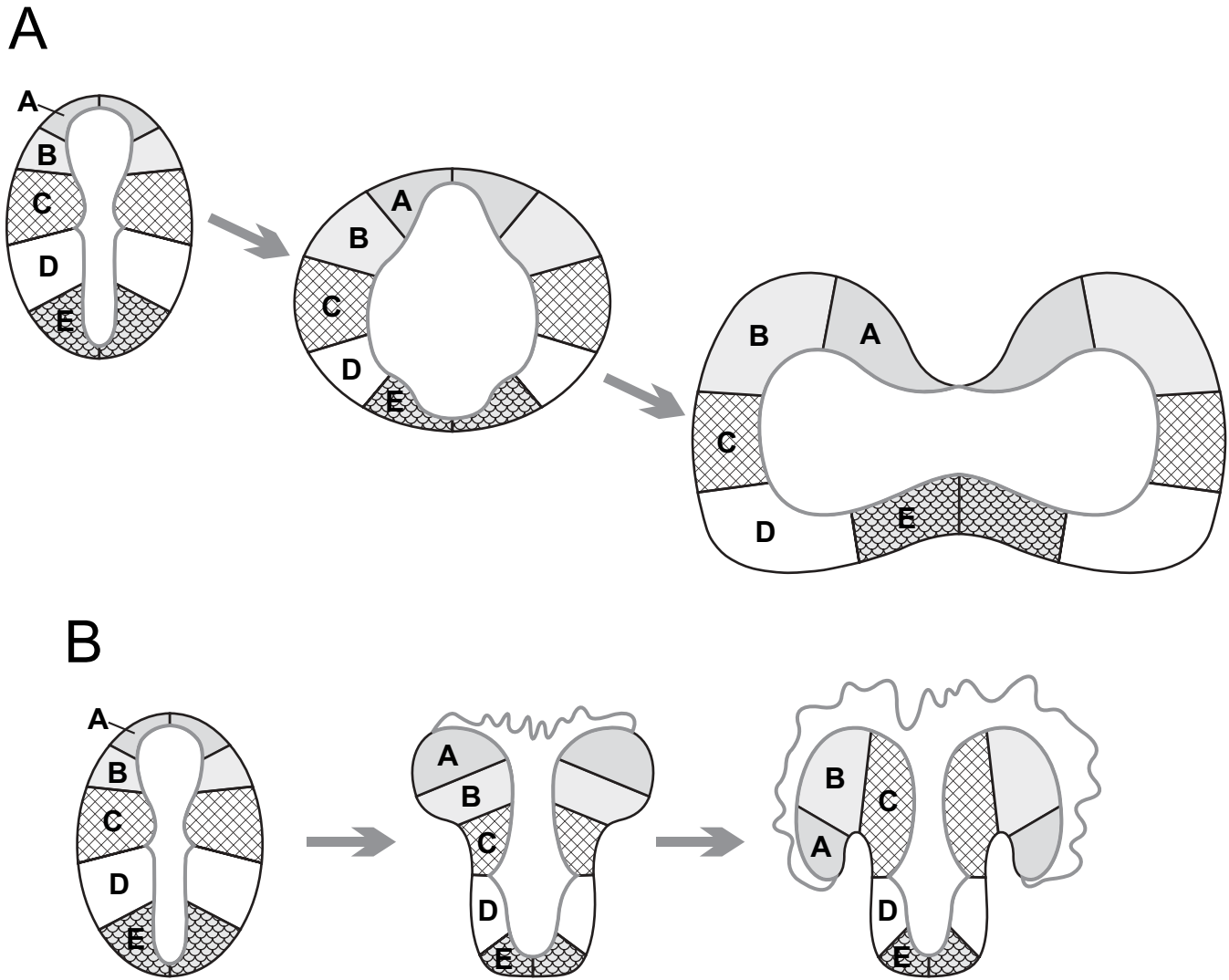


FIGURE 3-9. A: Diagram of the process of evagination in forebrain development, as occurs in most groups of vertebrates. B: Diagram of the process of eversion in forebrain development, as occurs in ray-finned fishes. In both sets of drawings, the ventricular surface is indicated by a gray line for ease of comparison between the evaginated and everted conditions. To emphasize the relative topological relationships, fewer divisions of the hemisphere are shown than actually exist. For example, the area labeled C consists of two pallial regions.

compare between them is still very much a matter of debate. In mammals [Fig. 3-10(A)], the dorsal part of the evaginated pallium forms part or all of the six-layered neocortex, while other parts form the medial (hippocampal) and lateral (olfactory) cortices. In the deeper part of the ventrolateral pallial region lies the **claustramygdalar formation**, which is also of pallial origin. It is composed of part of a diverse nuclear group called the amygdala and associated structures. In birds [Fig. 3-10(B)] and reptiles, part of the pallium forms the dorsal cortex, a cortical area between the medial (hippocampal) and lateral (olfactory) cortices. In birds, as shown in the figure, this region is called the **Wulst**, or the **hyperpallium**. Another part of the pallium forms a region that expands inward to form a large, nuclear area called the **dorsal ventricular ridge**. The

anterior part of the dorsal ventricular ridge (ADVR) was long thought to represent a huge, subpallial telencephalic area for use in stereotyped motor behaviors, but subsequent connective and histochemical studies eliminated that hypothesis from further consideration. These studies also indicated that the ADVR is homologous (as a collection of several embryologically derived fields) to several parts of mammalian neocortex. More recent findings, particularly from embryological studies, have suggested the alternative possibility that the ADVR is homologous to part or all of the claustramygdalar formation. A third possibility is that the ADVR is homologous as a field to both the claustramygdalar formation and parts of neocortex. These possibilities are discussed in much more detail in later chapters.

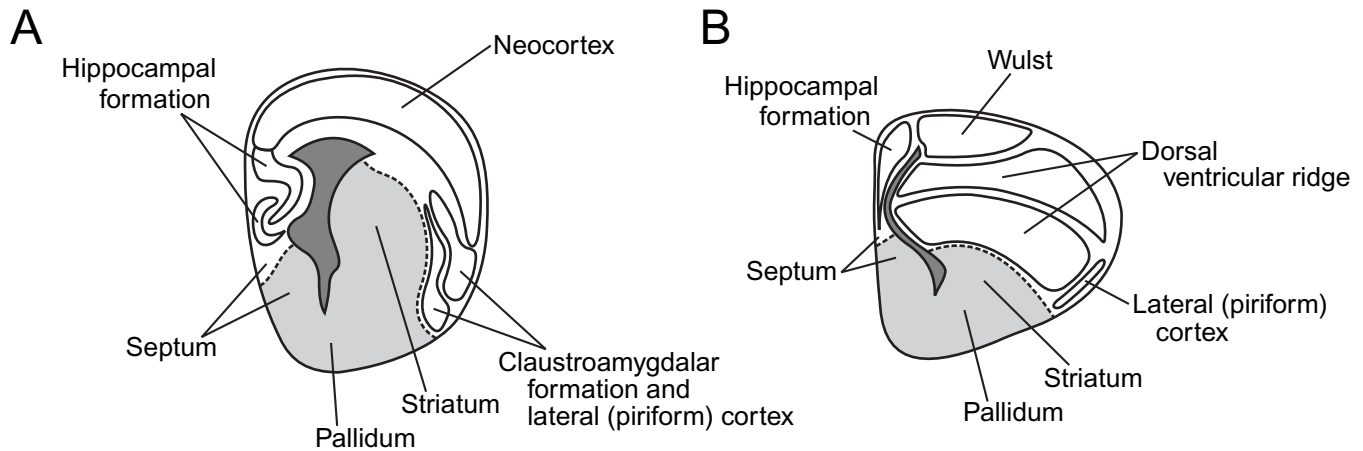


FIGURE 3-10. Diagram of transverse hemisections through the telencephalon to show the major pallial and subpallial regions in a mammal (A) and a bird (B). The ventricle is indicated by dark shading and the subpallium by lighter shading. In both the mammal and the bird telencephalon hemisections, all of the area in white is pallium.

The differences in the organization of both evaginated versus everted telencephalons and neocortex/claustroamygdalar formation versus the anterior dorsal ventricular ridge are differences of the topography of various groups of neurons. They arise from differences in the gross behavior of the pallial sheet as a whole and in the generation and migration patterns of pallial neuronal populations. As discussed above, growth cones of axons require various local guidance cues in order to grow along the right path and reach their target. Developing dendrites require the arrival of afferent axons within the proper time frame to continue developing and be maintained. Developmental differences can produce grossly different topographical relationships of areas in the telencephalon, but the other, multiple developmental factors necessary for the establishment of connections are generally unaffected and sufficient despite the alterations of topography in these cases.

Ontogeny and Recapitulation

In closing this section, there is one final aspect of brain development to consider briefly. One of the most pervasive of “old wives’ tales” is the notion that ontogeny recapitulates phylogeny: in other words, that the developmental sequence is a kind of rerun of the species’ evolutionary history. In the late 1800s, Haeckel promoted the idea that evolutionary change results from the addition of new ontogenetic stages to the terminal phase of the ancestor’s development. Such **terminal additions** to existing sequences of development would be the basis of ontogeny recapitulating phylogeny. Terminal additions do, in fact, occur in phylogeny, but the sequence of development in vertebrate brains does not recreate adult ancestral stages of the species’ evolutionary history.

From our analysis of differences in the development of the telencephalon, we can see that, for ontogeny to recapitulate phylogeny, particularly in terms of the now discredited *scala naturae* (see Chapter 1), a highly improbable series of events

would have to occur to produce the brain of an adult reptile or mammal. The telencephalic pallium would first have to evaginate, as in lampreys and cartilaginous fishes, then undo the evagination and evert as in ray-finned fishes, then undo the eversion and evaginate as in amphibians and amniotes. Nevertheless, attempts persist to perceive a recapitulation of phylogeny in ontogenetic sequences, as with long projection neurons developing before locally projecting ones and motor neurons before sensory ones. Many of these attempts are based on erroneous *scala naturae* thinking and also fail to take into account the multitude of features that were gained quite suddenly with the evolution of neural crest and placodes (see Chapter 9) in ancestral vertebrates.

As in many incorrect ideas, there nonetheless is a grain of truth in the ontogeny-phylogeny idea. In the early 1800s, Karl von Baer realized that developmental sequences do not recreate stages from “lower” to “higher” groups of animals. He did note, however, that resemblances occur among embryos within a group, and that the resemblances decrease as development proceeds. von Baer concluded that those features that are common to a group appear earlier in development than the more specialized features of individual taxa within the group. Thus, in the development of the brain of a seagull, for example, we would expect features common to chordates to develop first, followed by features common to all vertebrates, and so on in sequence through features common to jawed vertebrates, sarcopterygians, tetrapods, amniotes, birds, and finally seagulls. von Baer thus believed that over evolution, there is conservation of a number of developmental stages. This concept is referred to as “**von Baerian recapitulation**,” and a growing body of data supports it.

The von Baerian view makes sense when we note that adult phenotypes are produced by a series of ontogenetic sequences. Changes over evolution in the phenotype are the direct result of changes in the ontogenetic sequences, which in turn are produced by mutations established in the genome,

shifts in the timing during development of some events relative to others (**heterochrony**), and other developmental factors, as discussed in Chapter 1. Features that are common to all vertebrates, such as the neural tube, arise before more specialized features present only in one radiation, such as the dorsal ventricular ridge in nonmammalian amniotes. Given the complexity and interactions of developmental events, modifications in early sequences would have much more profound, and in most cases disruptive, effects than modifications in later sequences. The reduction of particular systems and the maintenance of neotenic (embryonic) characteristics in the adults of some groups may in fact result from relatively early modifications in the rates of cell proliferation, differentiation, and migration.

Although some of the later modifications constitute terminal or near terminal additions, the radiations of extant vertebrates have been separated long enough that such terminal additions reflect their independent histories rather than allowing for the construction of a single line of evolutionary history. Marked differences in the development of the telencephalon between as well as within the major vertebrate radiations clearly demonstrate the separateness and independence of the radiations over a long period of time. On the other hand, those features that are common to most or all groups, in developmental structures and sequences and in the adults, can be used to reconstruct the condition of the brain in the common ancestral vertebrate stock.

THE BRAIN AND SPINAL CORD

In the head region of early vertebrates, the elaboration of neural crest and placode tissues resulted in the formation of most of the paired sense organs and a new rostral (front) part of the head to house them. The central nervous system was likewise enlarged and elaborated so that it was able to play a greater role in sensory and motor integration. A new rostral part of the brain, called the telencephalon, was also added in which sensory information could be further analyzed, integrated, and remembered, allowing for sophisticated decision-making capabilities and for appropriate and learned motor responses to a variety of stimuli.

The central nervous system consists of the brain and the spinal cord. Figure 3-11 illustrates the location of the brain and the rostral end of the spinal cord in the head of an adult vertebrate, a lizard in this example, and demonstrates some of the standard terms of orientation (also see the Appendix). While the distinction between brain and spinal cord is of some importance in medical education and neurology, it suggests a much greater dichotomy of function than actually exists. Indeed, this subdivision is often confusing to newcomers to the neurosciences because it emphasizes the relatively few differences and directs attention away from the many similarities between the two regions.

The boundary between the brain and spinal cord is not nearly as sharp as some textbooks suggest, nor does it correspond precisely to the junction of the skull and the vertebral column (spinal column or backbone), which surrounds and protects the spinal cord. Although a substantial portion of the brain consists of unique structures that have no counterpart in

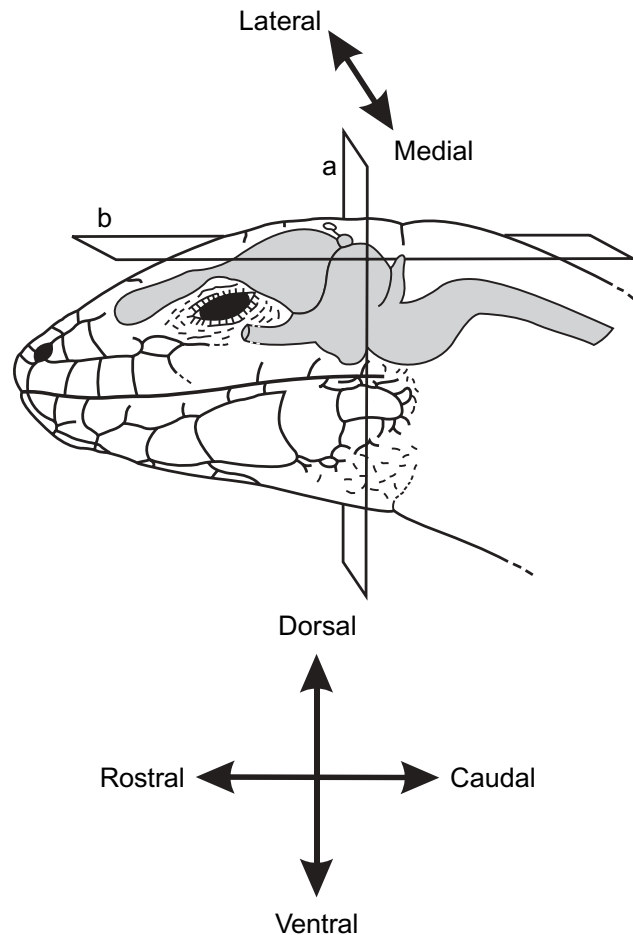


FIGURE 3-11. Lateral view of the head of a lizard (*Lacerta sicula*) with the position of the brain and the rostral part of the spinal cord (indicated by shading) shown *in situ*. Rectangle “a” represents the transverse plane, which runs from dorsal to ventral and medial to lateral. Rectangle “b” represents the horizontal plane, which is approximately parallel to the line of the mouth and runs from rostral to caudal and medial to lateral. The sagittal plane is parallel to the lateral view shown in the figure and runs from rostral to caudal and dorsal to ventral. Adapted from Senn (1979). Used with permission of Elsevier.

the spinal cord, much of the brain, especially its caudal region, is actually a continuation of the structures and general organization of the spinal cord.

The spinal cord is organized for the control of the body's limbs and trunk; similarly, the caudal brain is organized for the control of specialized structures in the head, such as the jaws, tongue, eye muscles and lids, and vocal organs. Moreover, the caudal brain and spinal cord share the task of control and regulation of the viscera, or internal organs, such as the heart, digestive system, and respiratory system.

CELLULAR ORGANIZATION OF THE CENTRAL NERVOUS SYSTEM

The cells in the brain and spinal cord are of two types: nonneural cells called glia, which fill in the spaces between

neurons and wrap around parts of neurons, and the neurons themselves. As discussed in Chapter 2, most neurons can be categorized into three broad categories—sensory afferent neurons, which are within the peripheral nervous system (PNS); efferent neurons, which have cell bodies within the central nervous system (CNS) but send their axonal processes out into the periphery; and all of the other neurons that lie within the central nervous system. The sensory afferent and the efferent neurons are both Golgi Type I cells, which have long projection axons. The sensory afferent neurons bring informa-

tion about the internal and external environments into the central nervous system. The efferent neurons are motor or effector cells that carry (either directly or via a second neuron in the peripheral nervous system) instructions from the central nervous system to the body's effector organs, the muscles and glands. The third category—the vast majority of the neurons that constitute the CNS—consists of both Golgi Type I and Golgi Type II cells. The Golgi Type I cells are sometimes referred to as **projection neurons** and the Golgi Type II cells as **local-circuit neurons** or **interneurons** (Fig. 3-12).

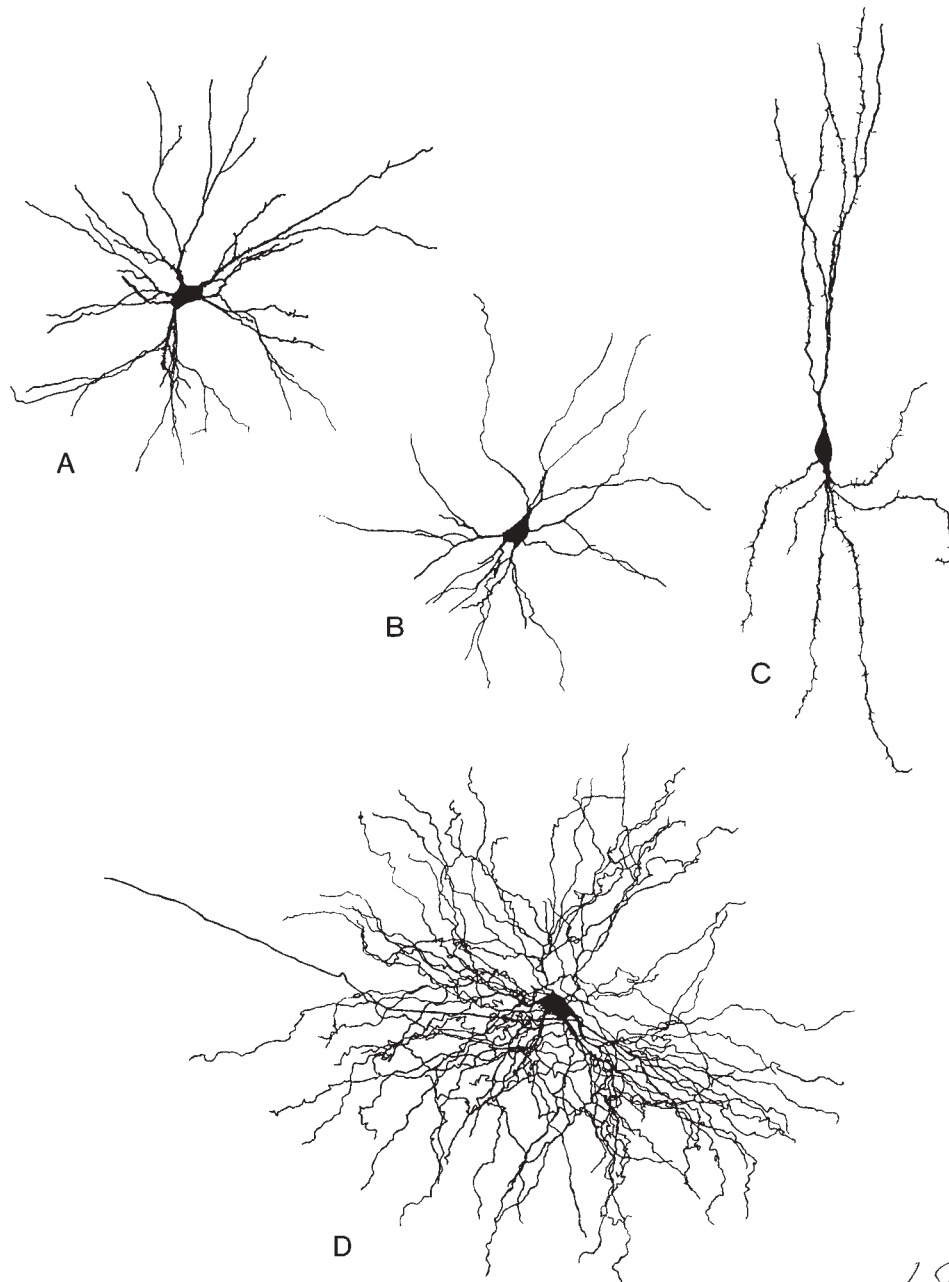


FIGURE 3-12. Examples of neurons found in the forebrain in various mammals, from the dorsal thalamus of a cat (A and B), after Robson (1993); from the cerebral cortex of a monkey (C), after Lund and Lewis (1993); and from the dorsal thalamus of a monkey (D), after Havton and Ohara (1993). Figures used with permission of John Wiley & Sons.

We should note that the terms “afferent” and “efferent” may be used in conjunction with the primary sensory and the motor or effector neurons, respectively, or in reference to the direction of information relay within the central nervous system. In the latter sense, afferent means “coming into,” and efferent means “going out of.” The axon of a Golgi Type I neuron that comes into and terminates within a specified neuronal population, which we will call A, is afferent to A. The axon of another Golgi Type I neuron that goes from A to a different neuronal population, which we will call B, is efferent from A and afferent to B.

The CNS intermediary neurons form a neural chain between the primary sensory afferent neurons and the efferent neurons. Rarely does a primary sensory neuron make direct contact with a motor neuron. Rather, a few or many thousands of other neurons typically receive the flow of information from sensory neurons into the central nervous system, process that information, and send the resultant outflow of instructions to muscles or glands via the effector neurons. The processing of information that is carried out within the CNS determines whether the instructions will be for action or for inaction and whether a response will be rapid or leisurely, vigorous or delicate, toward an object or away from it.

This general description of central nervous system organization applies to both the spinal cord and brain. The rostral-most parts of the brain have fewer primary sensory, afferent components and fewer effector, efferent components than are present in the brainstem. The rostral brain consists mostly of neurons arranged in a variety of specialized Golgi Type II local-circuit populations that are interconnected by long-axon, Golgi Type I projection neurons. Ascending projections from nuclei in the brainstem bring sensory information and also feedback information up to the rostral brain, and descending projections from the rostral brain carry its output. The heavy concentration of neurons in the rostral brain has served to focus attention on this region as the possible “executive” component of the central nervous system, with major responsibilities for decision making, memory, attention, communication, emotion, and other important, complex behavioral processes.

To summarize, the brain and spinal cord are organized to allow for the input of primary sensory information, the analysis and processing of the information, and the production and transmission of appropriate responses to the information. The axons of incoming, primary sensory, afferent neurons bring sensory information into the brain and spinal cord. Long-axon, projection (Golgi Type I) neurons carry this information between multiple nuclei and cortices. Short-axon, local circuit (Golgi Type II) neurons within nuclei and cortices are involved with processing the information. Additional sets of projection neurons carry the output for responses to the outgoing motor or effector neurons in the brain and spinal cord.

for regions of the spinal column through which the spinal nerves exit on their way to the various parts of the body. Thus, the region of the cord from which nerves exit through the cervical (neck) bones is called the **cervical cord**. This is the most rostral division of the cord and is continuous with the most caudal region of the brain.

Proceeding caudally within the spinal cord, the remaining divisions are the **thoracic** (chest) **cord**, the **lumbar** (abdominal) **cord**, and the **sacral** (pelvic) **cord**. All along its length, the spinal cord communicates with the body via a series of **spinal nerves**. The dorsal part (alar plate) of the spinal cord receives incoming, primary sensory fibers known as **general somatic afferent** fibers from the skin, muscles, and joints of the neck, body, limbs (if any), and tail (if any). It also receives sensory fibers from the viscera known as **general visceral afferent** fibers. Likewise, the ventral part (basal plate) of the spinal cord sends out motor fibers (axons) that control the muscles of these body parts. The latter are known as **general somatic efferent** fibers.

From the thoracic and lumbar regions of the cord, a different group of efferent neurons influences the innervation of the smooth muscles of the digestive system and other internal organs and glands. This influence is carried out via a relay through a second set of effector neurons in the peripheral nervous system. The central nervous system neurons for this system are known as **general visceral efferent** fibers. The subset of the general visceral efferents that lie in the thoracic and lumbar spinal cord are known as the **sympathetic nervous system**. They function to provide a rapid activation of various internal organ systems such as the cardiovascular and respiratory systems when severe demands are placed on these systems or in times of emergency when quick action is required. This system serves “fight or flight” and related responses.

The sympathetic nervous system is complemented by another general visceral efferent system, the **parasympathetic nervous system**, which is composed of visceral efferent neurons from the sacral division of the spinal cord and from the caudal regions of the brain. The parasympathetic system controls (via a second set of effector neurons in the peripheral nervous system) the same organs as does the sympathetic system, but it does so under normal conditions, when no special stresses are present. This system functions in promoting the digestion of food, allowing urination to occur, and other related, normal functions of the organs. Thus, when a high-demand situation arises, the sympathetic system takes control; when the high-demand situation ceases, control returns to the parasympathetic system. The sympathetic and parasympathetic systems together are known as the **autonomic nervous system**.

The Brain

Figure 3-13 is a drawing of the brain and rostral spinal cord of a vertebrate, in this case a ray-finned fish, which will serve as an example for the general organization of vertebrate brains. Each of the lobes and other swellings of the brain surface has a specific name, as briefly introduced above, such as the mid-brain roof (tectum) or cerebellum. Groups of lobes or swellings are known by regional names, such as the mesencephalon

REGIONAL ORGANIZATION OF THE NERVOUS SYSTEM

The Spinal Cord

Both the brain and spinal cord can be subdivided into individual regions. The subdivisions of the spinal cord are named

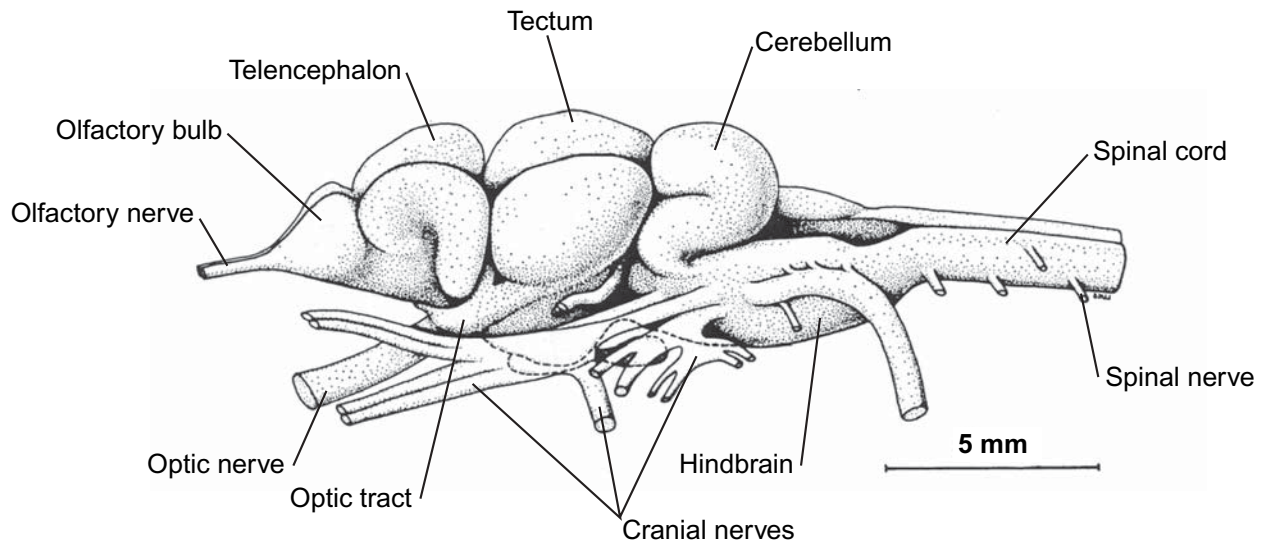


FIGURE 3-13. Drawing of a lateral view of the brain of a ray-finned fish, the longnose gar (*Lepisosteus osseus*). Rostral is toward the left. Adapted from Northcutt and Butler (1976).

(midbrain). Still more-encompassing regional names are used, such as forebrain and brainstem.

The nerves entering and leaving the brain are the **cranial nerves**. Like the spinal nerves, the cranial nerves carry primary sensory afferent axons (mainly from the head rather than the body) into the central nervous system and the axons from motor or effector efferent neurons that control the muscles and glands of the head and neck. Although these nerves are given special names, such as trigeminal nerve or oculomotor nerve, the organization of at least some of them is essentially the same as that of the spinal nerves. Moreover, some of the neuronal populations (nuclei) of the more caudal cranial nerves are directly continuous as a cell column with equivalent cell populations in the spinal cord.

Hindbrain. The caudal-most region of the brain is the **rhombencephalon**, or **hindbrain**, which comprises the **myelencephalon**, or **medulla oblongata**, and the **metencephalon**, which consists of the **pons** and **cerebellum**. The cranial nerves of this area include motor efferents that innervate the muscles of the jaws and the superficial facial muscles, such as those of the lips, cheeks, and forehead, the muscles of the tongue (where present) and throat, and one of the extraocular muscles of the eyeball. They also include components that comprise most of the cranial division of the parasympathetic nervous system. On the sensory side, some senses that traditionally have been called “special senses” are represented by cranial nerves that enter the brain at this level. Such special senses are those that are unique to the head region, such as hearing and the sense of balance and acceleration (vestibular sense). Other so-called special senses, not present in all vertebrates, include the lateral line system for the detection of water displacement over the body surface and of electric fields in the aquatic environment and the infrared (IR) sense for the detection of body heat radiated by other animals. The general senses of touch, position, temperature, and pain for much of the head region are also afferent to hindbrain sensory nuclei.

In addition to the nuclei associated with some of the cranial nerves, the medulla and pons contain other nuclei and a number of fiber tracts. Many of the fiber tracts are long pathways between the spinal cord and the more rostral parts of the brain, while others are shorter and run between nuclei within this area. Some of the cell populations in the medulla and pons are more widely scattered and diffuse than most other nuclei in the brain. These scattered populations are collectively referred to as the **reticular formation**. The nuclei of the reticular formation are involved in integrating inputs from a variety of sources, including the cranial nerve nuclei and more rostral parts of the brain. The reticular formation regulates and modulates activities elsewhere in the brain on the basis of the incoming information. A transverse section through the hindbrain in a fish (Fig. 3-14) illustrates the distribution of nerve cell bodies within this part. Fiber tracts run in the areas in which there are few or no cell bodies. Closely related to the pons, both geographically and functionally, is the cerebellum (Fig. 3-13). The **cerebellum** is a cortical structure in the roof of the hindbrain. Among its other functions, the cerebellum is involved in balance, coordination, and the smooth execution of rapid movements.

Midbrain. The next major subdivision of the brain is the **mesencephalon** or **midbrain**. The most prominent external feature of this area in most vertebrates is the roof of the midbrain, or **tectum** (Fig. 3-13). This structure is also often referred to as the **optic lobe**, or **optic tectum** (Fig. 3-14), due to the large number of neurons of the optic nerve that terminate within its superficial layers. The ventral portion of the mesencephalon, the region underneath the tectum, is known as the **tegmentum**. The mesencephalic tegmentum contains a number of nuclei and fiber tracts, including the nuclei of two motor cranial nerves that innervate most of the extraocular muscles for control of eye movements. The operation of the intraocular eye muscles, which mediate constriction of the pupil and the focus of the lens, is controlled from this

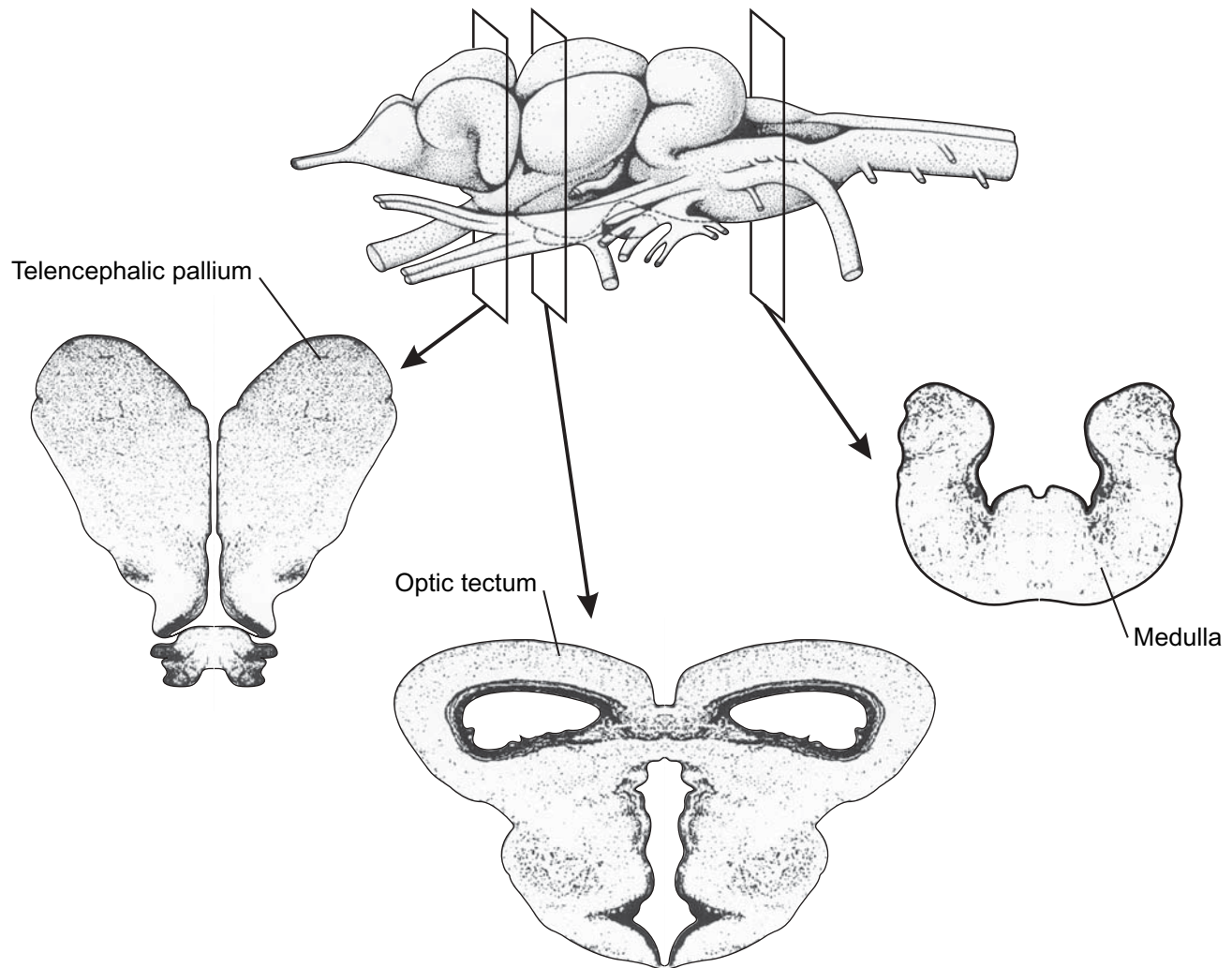


FIGURE 3-14. The brain of the longnose gar, as shown in Figure 3-13, with transverse sections through the telencephalon, midbrain, and hindbrain. Adapted from Northcutt and Butler (1976).

region as well via parasympathetic efferent fibers. The midbrain does not directly receive any afferent cranial nerve components.

Forebrain. The **prosencephalon**, or **forebrain**, is the most rostral division of the brain. It contains two major parts: the **diencephalon** and the **telencephalon** (Fig. 3-13). The diencephalon, not labeled in the figure, lies rostral to the midbrain, caudal-ventral to the telencephalon, and medial to the axons that form the optic tract, the central nervous system continuation of the optic nerve. The diencephalon is a large division composed of six principal areas. The caudal part of the diencephalon contains a dorsal area called the **pretectum** and a more ventral area called the **posterior tuberculum**. More rostrally, four areas are present. In dorsal to ventral sequence, these areas are the **epithalamus**, the **dorsal thalamus**, the **ventral thalamus**, and the **hypothalamus**. Each of these areas is composed of a number of nuclei, and there are also

major fiber tracts that pass through this region. In contrast to the midbrain, the forebrain receives sensory afferent information and does not give rise to any cranial nerve effector components.

A number of the nuclei in the pretectum receive visual input from the retina and are involved in visuomotor behaviors. Pretectal nuclei and other visually related nuclei in the tegmentum influence eye movements (via midbrain and hindbrain motor nuclei) in relation to prey and predator detection and to orientation of the body within space. The posterior tuberculum consists in part of a medially lying nucleus that contains neurons involved in regulating motor functions. In ray-finned fishes, more laterally lying nuclei of the posterior tuberculum are also present. These nuclei relay sensory inputs (from hindbrain sensory nuclei) to the telencephalon. Similar nuclei may be present in cartilaginous fishes, but migrated posterior tubercular nuclei have not yet been identified in amphibians or land vertebrates.

The epithalamus contains the **epiphysis** (**pineal gland** and related structures), which is located at the end of a stalk, the **epiphyseal stalk**. In some animals, such as reptiles, the pineal is a structure very similar to the eye. It contains light receptors and gives rise to primary sensory afferent neurons, which terminate in the epithalamus. In mammals and birds, the pineal is a glandular structure. The epithalamus also contains the **habenula**, which comprises the habenular nuclei and is present in all vertebrates.

The nuclei in the dorsal thalamus receive information via projection neurons from the various sensory systems, which they transmit to various parts of the telencephalon. The nuclei in the dorsal thalamus constitute a gateway to the sensory areas of the telencephalon. A number of different parts within the telencephalon are involved in integrating the incoming sensory information for learning, memory, emotional responses, and motor responses. In some vertebrates—particularly in mammals and to some extent in birds—the dorsal thalamic nuclei also receive reciprocal projections from their major telencephalic target. The nuclei that lie in the ventral thalamus are involved in modulating the activity of dorsal thalamic nuclei and also play a role, in concert with telencephalic structures, in motor control of the body and limbs.

The hypothalamus is extensively involved in the activities of the autonomic nervous system and the endocrine system. It controls the endocrine system's production of hormones by means of the **hypophysis**, or **pituitary**, which is directly connected to the hypothalamus. The pituitary is located at the end of a stalk, the **infundibulum**, which is a direct outgrowth of the base of the hypothalamus. The hypothalamus thus is able to control and regulate behavior patterns that depend on the levels of hormones in the blood, such as sexual behavior, parental behavior, territoriality, migration, and hibernation, to name but a few. The hypothalamus also is concerned with feeding and drinking, aggression, temperature regulation, and a number of other important biological and behavioral functions.

The most rostral region of the brain, the **telencephalon** (Figs. 3-13 and 3-14), includes an upper part, the **pallium**, which includes the **cerebral hemisphere** (also called the **cerebrum**). At the rostral end of the cerebrum is the **olfactory bulb**, in which axons of olfactory receptor cells in the nasal mucosa terminate. In animals in which the sense of smell is highly developed, such as some sharks and bloodhounds, the olfactory bulb is rather impressive in size. In animals such as many birds and some mammals, in which the sense of smell is not especially important for survival, the bulb is relatively small in comparison. The olfactory bulb projects to the olfactory part of the pallium in the telencephalon via **olfactory tracts**, which can be short if the olfactory bulb lies adjacent to the telencephalon (as in the brain of the fish shown in Fig. 3-13) or elongated.

The cerebrum itself has a relatively smooth surface in most vertebrates. It is composed of nuclear areas in some vertebrate groups, such as cartilaginous and most ray-finned fishes; in other vertebrate groups, particularly tetrapods, it is composed of both nuclei and cortex. In some animals, mostly among the mammals, although there are other instances as well, the surface of the cerebrum develops ridges and valleys known as convolutions. The ridges are called **gyri** (singular = **gyrus**) and

the valleys are called **sulci** (singular = **sulcus**). The deepest of the sulci are known as **fissures**. Among mammals, gyri and sulci tend to be present in those species within each genus that have larger body and brain size in absolute terms, and these hemispheres are described as **gyrencephalic**. In contrast, the smaller species within each mammalian order have few or no gyri and sulci. The smooth surface of their hemispheres is described as **lissencephalic**. Most of the surface of the cerebrum, whether lissencephalic or gyrencephalic, is occupied by the neocortex.

The telencephalon also includes several other major areas. The **hippocampus** comprises several cortical regions; it is necessary for memory and is also involved in emotion. The hippocampus and some nuclei related to it, including the **septal nuclei** and parts of the **amygdala**, receive olfactory and other sensory information. The adjective **limbic** is a somewhat general term that can be applied either to the hippocampal formation and its connectionally related structures but not including primary olfactory structures or to both hippocampal and primary olfactory structures. Several additional major areas lie in the more ventral part of the telencephalon, the **subpallium**, and are involved with motor functions. These areas include part of the amygdala and a set of nuclei that are collectively called the **basal ganglia**. The latter include the **striatum** and the **pallidum**. (Note the crucial distinction between “pallium” and “pallidum.”) The subpallial striatal and pallidal components are interconnected with motor areas of the pallium and with nuclei in the more caudal parts of the brain.

To conclude this section on an overview of the brain and its major components, an additional note on terminology should be made. A neuroanatomical term frequently encountered is **brainstem**. This term sometimes refers to the more ventral parts of the brain except for any part of the telencephalon, that is, to the medulla and pons, the midbrain tegmentum, and the diencephalon. Sometimes it even includes some or all of the subpallial structures in the telencephalon. It is alternatively used to refer only to the medulla, pons, and midbrain tegmentum (and sometimes the midbrain tectum) without including the diencephalon. Context must be used to determine the specific sense in which this somewhat loose term is being discussed.

The Meninges and the Ventricular System

The brain and spinal cord are covered by one or more layers of connective tissue, which are called the **meninges**, from the Greek word **meninx**, which means membrane. In fishes, only a single layer, the **primitive meninx**, is present. Amphibians and reptiles have two meningeal layers, an outer **dura mater** (meaning “hard mother”) and an inner thin layer, the **secondary meninx**. In mammals and birds, three meningeal layers are present. The layer closest to the brain is a thin layer called the **pia mater** (meaning “tender mother”). The middle layer is a thin, avascular layer called the **arachnoid** due to its spider web-like appearance. The space between the pia mater and the arachnoid is the **subarachnoid space**. Blood vessels lie within it. The outermost layer is the **dura mater** and is actually composed of two layers: an inner layer enclosing the central nervous system and an outer layer that lines the inside of the skull. The use of the word “mother” to describe these

membranes comes from an ancient notion that they were the origin, or mother, of all membranes in the body.

As discussed above, the central nervous system develops embryologically from a hollow tube. The walls of the tube thicken to form the brain and spinal cord, and the hollow within the tube becomes the fluid-filled **ventricular system** of the adult. Instead of remaining a straight tube of uniform diameter, the ventricular system extends laterally into the variously expanded parts of the brain in different vertebrate groups, such as the olfactory bulbs, telencephalic hemispheres, the midbrain roof, and/or the cerebellum. This arrangement is shown in Figure 3-15.

In most groups of vertebrates, the ventricular system expands laterally within each of the telencephalic hemispheres, and this pair of laterally extending spaces is called the **lateral ventricles**. The lateral ventricles are in continuity, through paired openings called the **interventricular foramina of Monro**, with the unpaired, medial ventricular space of the diencephalon, called the **third ventricle**. The caudal continuation of the third ventricle is a narrow canal called the **cerebral aqueduct of Sylvius**, which in turn opens into the **fourth ventricle**, the unpaired, medial ventricular space of the hindbrain. Viewed from its dorsal aspect, the fourth ventricle has a rhombic shape (that of a parallelogram), giving the rhombencephalon its name. The fourth ventricle is caudally continuous with the **central canal** of the spinal cord.

Parts of the ventricular walls consist of a thin ependymal epithelial layer and the pia mater, which together form the **tela**

choroidea. A network formed by blood vessels and the tela choroidea, called the **choroid plexus**, secretes **cerebrospinal fluid** into the ventricular spaces. The cerebrospinal fluid circulates in the ventricular system and also in the subarachnoid space; it reaches the latter by passing through three openings that connect the fourth ventricle with an enlarged part of the subarachnoid space, the **cisterna magna**. The three openings are a paired set, the **foramina of Luschka**, one at each lateral aspect of the ventricle, and an unpaired, medial foramen, the **foramen of Magendie**. After circulating, the cerebrospinal fluid passes out of the subarachnoid space into vascular sinuses through structures in the arachnoid called **arachnoid villi**, which act as one-way, pressure-sensitive valves. The cerebrospinal fluid provides support for the brain and cushions it from physical shocks by its buoyancy.

MAJOR SYSTEMS OF THE BRAIN

We now want to give you a very brief overview of some of the major systems of the brain. As we have discussed above, there are major sensory and motor systems in which information is relayed through various nuclei, being modified and sorted along the way. In later chapters, which cover various parts of the brain, a general idea of the basic organization of these systems will help you to make sense of the anatomy.

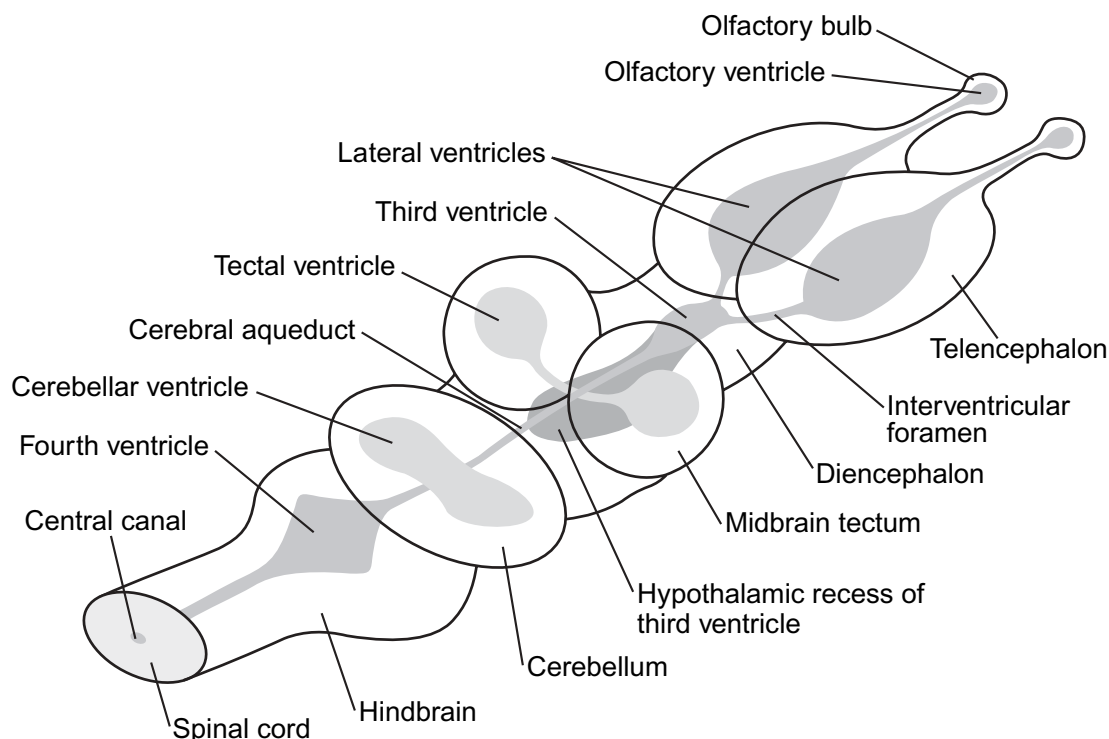


FIGURE 3-15. Dorsolateral schematic drawing of a generalized ray-finned fish brain to represent the general vertebrate condition of the ventricular system, indicated by shadings. Not all vertebrates have a hypothalamic recess of the third ventricle or tectal or cerebellar ventricles. Rostral is toward the upper right.

Sensory Systems

All of the receptors for touch and position sense, radiant-energy sense, pain and temperature, lateral line (for wave displacement and electrical field detection), hearing, vestibular sense, and gustatory sense have their initial points of termination within the central nervous system either in the spinal cord or in the hindbrain (in the medulla and/or pons). As mentioned in Chapter 2, the target cell populations of these primary pathways can be referred to as **first-order multipolar neurons (FOMs)**, since they are the first of several groups of multipolar neurons that form the sensory pathway within the central nervous system. The FOMs receive the sensory bipolar neuron inputs and then project to more rostral levels of the brain, particularly the dorsal thalamus and the optic tectum, which itself then projects to the dorsal thalamus as well. Similarly in the visual system, retinal bipolar neurons receive receptor inputs and terminate on retinal ganglion cells, which are the FOMs for the visual pathways. Most of the retinal ganglion cell axons terminate in part of the dorsal thalamus and in the optic tectum. From the dorsal thalamus, the various pathways project to part(s) of the telencephalic pallium, and, in some cases, to part of the subpallium as well. The olfactory pathways, in contrast to the more caudal sensory pathways, project directly into part of the telencephalon. Topographic organization is an important characteristic of all of these pathways; this feature provides for orderly maps of the sensory input within particular parts of the brain that correspond to the spatial map of the external world.

Each of the ascending sensory pathways to the telencephalic pallium terminates in its own segregated region. From that site begins the complex and varied series of possible pathways that are the routes to other sensory, integrative, and motor systems. Functions including memory storage of sensory events and the consequences of reactions to them, decision making about subsequent reactions to such events, and the conscious awareness of these events reside to a large extent within the telencephalon. In order to gain a general understanding of how ascending sensory systems are organized in their projections to the pallium, we will briefly outline three of them here, as based on the mammalian condition: the auditory, visual, and somatosensory pathways.

The Auditory Pathway. In the auditory pathway, axons arise from neurons in the inner ear and pass into the brain in the **eighth (octaval) cranial nerve**. These axons project to an auditory nucleus in the hindbrain [Fig. 3-16(A)]. The neurons in this nucleus give rise to a tract (called the **lateral lemniscus**) that terminates on neurons within a part of the midbrain roof called the **torus semicircularis** in most vertebrates and the **inferior colliculus** in mammals. The torus semicircularis lies ventral and/or caudal to the optic tectum. Neurons within the torus semicircularis project to an auditory nucleus in the dorsal thalamus. The latter nucleus projects, via tracts called the **forebrain bundles**, to one or more auditory regions of the pallium.

The Visual Pathways. Neurons in the retina give rise to axons that enter the brain via the **optic nerve** [Fig. 3-16(B)] and its continuation, the **optic tract**. Most retinal axons ter-

minate on neurons located either in the optic tectum of the midbrain (called the **superior colliculus** in mammals) or in a visual nucleus in the dorsal thalamus. Visual neurons in the optic tectum also project to a second visual nucleus in the dorsal thalamus. Each of the two visual dorsal thalamic nuclei projects to the telencephalon via the forebrain bundles and terminates in one or more visual areas within the pallium.

The Somatosensory Pathways. Axons that carry somatosensory information [Fig. 3-16(C)] enter the spinal cord and pass rostrally to terminate on neurons within two cell groups called the **dorsal column nuclei**. These nuclei lie in the junctional area between the spinal cord and the brainstem. Neurons in the dorsal column nuclei give rise to axons that pass rostrally in a tract called the **medial lemniscus**. Some of these axons terminate on neurons in a somatosensory part of the midbrain tectum. Other somatosensory axons from the dorsal column nuclei bypass the midbrain and terminate in a somatosensory nucleus in the dorsal thalamus. Neurons in the somatosensory part of the midbrain also give rise to projections to a second somatosensory nucleus in the dorsal thalamus. Each of the two dorsal thalamic somatosensory nuclei projects to the telencephalon via the forebrain bundles and terminates in two or more somatosensory areas within the pallium.

In the telencephalon, sensory information is relayed through multiple sets of projection (Golgi Type I) and local circuit (Golgi Type II) neurons—to secondary, tertiary, and further sensory and association pallial areas, into the limbic system for memory, into multisensory association pallial areas for integration, and so on. When the information has been processed and assimilated, appropriate motor responses follow.

Motor Systems

Complex control mechanisms for motor responses derive from neurons in the pallial motor areas of the telencephalon and/or from neurons in other dorsally lying structures, such as the roof of the midbrain and the cerebellum. Motor responses are also regulated by a number of structures, including the **striatopallidum** (striatum and pallidum), also known as the basal ganglia, in the lateral part of the telencephalic subpallium [Fig. 3-16(D)] and nuclear areas within the diencephalon, mesencephalon, and hindbrain. Mammals, for example, have motor neurons in the motor parts of the neocortex in the telencephalon that project to the striatum. In turn, neurons within the striatum project to the pallidum, which gives rise to feedback loops to the pallium via the dorsal thalamus and also to axons that pass caudally and terminate within a number of nuclei in the brainstem, including a nucleus in the pretectum [Fig. 3-16D] of the diencephalon. Neurons in the latter nucleus project to the midbrain tectum, which itself gives rise to descending motor projections to the brainstem and spinal cord.

Other neurons within the motor part of the pallium project caudally via the same major bundles in which sensory axons ascend—the forebrain bundles. These axons collectively form a tract that is rather like a major interstate highway. They pass caudally to synapse within nuclei in the midbrain and the brainstem and, in some cases, directly on neurons in the spinal cord. The latter, direct tract is present in mammals and is called

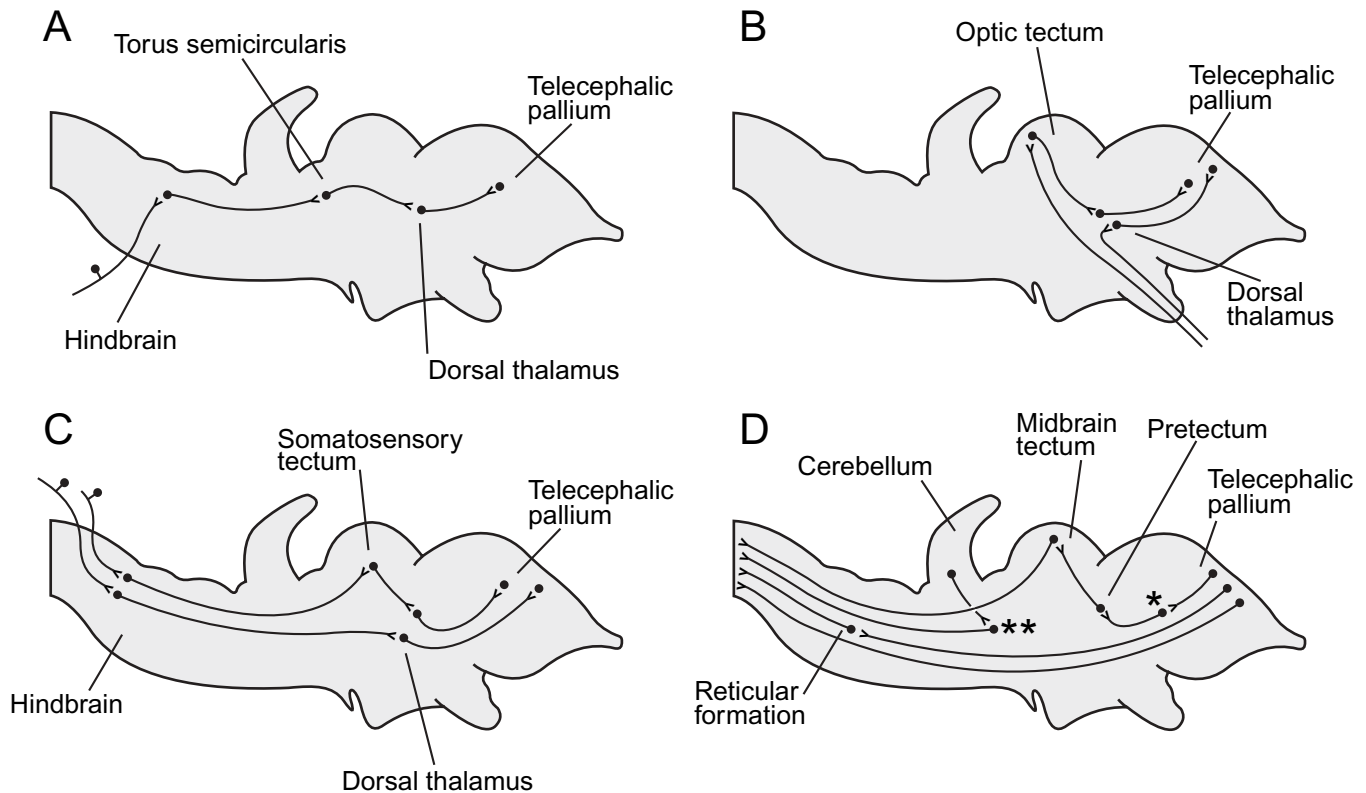


FIGURE 3-16. Schematic representation of the major sensory and motor pathways. Rostral is toward the right. Dots represent neuronal cell bodies, and lines represent the axons of the cell bodies with their terminal endings. Dendrites of cell bodies, on which the axons actually synapse, are not represented. (A) Ascending auditory pathway; (B) the two ascending visual pathways; (C) the two ascending somatosensory pathways; and (D) some of the descending motor pathways. In D, the uppermost descending pathway is from the pallium to the striatopallium (*) and then to the pretectum, midbrain tectum, and spinal cord. Also shown are the pathway from the cerebellum to the red nucleus (***) and then to the spinal cord, the corticoreticular and reticulospinal tracts, and the direct corticospinal tract (lowermost).

the **corticospinal tract**. Motor nuclei of the cerebellum similarly contain neurons that project to brainstem nuclei, particularly the vestibular nuclei and the red nucleus. The latter nuclei project to the spinal cord via the **vestibulospinal tract** and the **rubrospinal tract**, respectively. The reticular formation of the brainstem is composed of a number of different nuclear areas that also are involved in these descending motor pathways. Like the red nucleus, it receives pallial input and gives rise to descending projections to the spinal cord, in this case called the **reticulospinal tract**.

NOMENCLATURE OF THE BRAIN

Just as brains evolve, so too does the nomenclature that humans apply to its structures. Some of the nomenclature of the founding comparative neuroanatomists has been replaced with new terminology during the past several decades. The early comparative neuroanatomists include many illustrious workers, whose legacy is only sometimes given the great respect that it merits. To name just a few here, some of the earliest workers (19th century into the early 20th century) include S. Ramón y Cajal and his brother, P. Ramón, as well as

J. Bellonci, G. Cuvier, S. J. deLange, L. Edinger, G. Elliott Smith, S. P. Gage, C. Golgi, C. L. Herrick, W. His, O. D. Humphrey, H. Kuhlénbeck, W. A. Locy, A. Meyer, F. Pinkus, H. Rabl-Rückhard, W. M. Shanklin, and L. Stieda. Those whose contributions came mostly within the first half of the 20th century include C. U. Airèns Kappers, J. A. Armstrong, N. Beccari, J. Cairney, E. H. Craigie, E. C. Crosby, A. O. Curwen, A. Durward, T. Edinger, A. Frederikse, M. J. Gisi, F. Goldby, C. J. Herrick, M. Hines, N. Holmgren, G. C. Huber, J. B. Johnston, O. Larsell, R. N. Miller, M. Rose, P. Röthig, and R. E. Sheldon. Much of their nomenclature has stood the test of time and continues to be used, particularly those terms that are accurately descriptive and do not imply an incorrect homology. Many of the earlier workers also are represented in the terminology by eponymous terms—such as the nuclei of Bellonci, Darkschewitsch, Luys, Meader, and Meynert—a practice that is sadly dying out.

A substantial number of other terms have become problematic for one or more reasons and have been replaced. Forebrain structures in particular have undergone name changes; the diversity of the forebrain within and across different vertebrate radiations is arguably more pronounced than in most other parts of the brain, and thus its structures have been subject to misnomers based on incorrect assumptions of

homology. In some cases, particularly among fishes and amphibians where homologies are still largely unresolved, one of several sets of terms proposed in early work has become established through wide usage and the others have fallen into disregard. Within amniotes, nomenclature implying incorrect homologies has been the largest problem. For almost a century, it had been assumed that a very large proportion of the telencephalon of reptiles and birds, including the dorsal ventricular ridge (DVR), was homologous to the basal ganglia of mammals, which are involved in the initiation and control of voluntary movements, as well as in the suppression of unwanted ones. A sea change in our understanding of the telencephalon began with the work of Harvey Karten in the mid-1960s, when he demonstrated that the enzyme acetylcholinesterase was restricted to a much more ventral region of the telencephalic hemisphere of the pigeon than previously predicted. A relatively high level of this enzyme is a marker for the striatal part of the basal ganglia territory, particularly within amniotes, and its relative paucity in the DVR was highly surprising. Based on this and other findings, it was realized that the DVR was a component of the upper part of the telencephalon, or pallium, rather than part of the basal ganglia in the subpallium. The boundary between the pallium and subpallium had to be redrawn. Also, the relationship of the DVR to structures within the pallial part of the mammalian brain became a subject of debate that continues to the present time.

The terminology of components of the DVR has had a different history in reptiles and birds. The term dorsal ventricular ridge itself was introduced by J. B. Johnston in 1915. However, in some reptiles and in birds, various components of the DVR and/or other pallial areas were labeled with terms that included the suffix "striatum" in at least some of the early work, in keeping with the prevailing view that these areas were part of the basal ganglia. Such terms included "hyperstriatum," meaning "above the striatum," "neostriatum," meaning the "new striatum" and referring to the assumed homology with a similarly named part of the mammalian striatum, and "ectostriatum," meaning "out of the striatum." The "striatum" suffix died out in usage for these regions in reptilian telencephalons in the late 1960s, with reversion to Johnston's DVR term in most cases.

In birds, however, the use of the "striatum" suffix for some pallial areas persisted until very recently. This usage resulted in considerable communication problems between researchers working on different taxa of vertebrates, particularly those not well acquainted with the comparative nonmammalian literature. Recognizing this problem, Martin Wild and Anton Reiner proposed that a new set of terms be developed for the pallial regions in question and initiated a process that culminated several years and many discussions later with the Avian Brain Nomenclature Forum, which was organized by Erich Jarvis and held at Duke University in the summer of 2002. From this conference and the combined efforts of all its participants, a new nomenclatural system for the avian telencephalon was devised and published in two papers by Reiner et al., 2004 in the *Journal of Comparative Neurology*. The new nomenclature includes changes for some brainstem structures as well as for both pallial and subpallial regions of the telencephalon. The new terms either reflect well-established homologies or are neutral, descriptive terms that avoid promulgating disproved and discarded hypotheses of homology. The new nomenclature

will be introduced in appropriate places throughout this text, and comprehensive tables of the new terms are presented in Chapters 15 and 19.

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4

Vertebrate Phylogeny and Diversity in Brain Organization

INTRODUCTION

Animals in the phylum **Chordata** are characterized by the presence of a notochord, a dorsal nerve cord, and gill slits. Extant chordates (Fig. 4-1) comprise three major groups: **urochordates** (tunicates, or sea squirts), **cephalochordates** (represented by *Branchiostoma*, previously known as *Amphioxus*), and **vertebrates** (or **craniates**). The four major, extant vertebrate radiations are the cyclostomes, or agnathans, which comprise hagfishes and lampreys, and three radiations of jawed vertebrates, or **gnathostomes** (Fig. 4-2). Gnathostomes comprise **chondrichthyans** (ratfishes, sharks, skates, and rays), **actinopterygians** (ray-finned fishes), and **sarcopterygians** (fleshy-finned fishes and their four-limbed derivatives, the **tetrapods**). Most of the vertebrate taxa are **anamniotes**, that is, their embryos lack an amniotic membrane. **Amniotes**, in contrast, have an amniotic membrane that encases the embryo in amniotic fluid during development, freeing amniote vertebrates from the need to lay their eggs in water for development; amniotes are the land vertebrate (i.e., nonamphibian tetrapod) descendants of ancestral sarcopterygians.

Within each of the various vertebrate radiations, descendants of the ancestral forms have become diversified independently. Each species has some traits inherited from its ancestors, and most species also have specialized traits acquired through natural selection in changing environments. Specialized features can occur in any of the systems of the body, including the central nervous system.

Selective pressures may be many and diverse, but some general ones are active on most populations. Reproductive advantages may be gained by better avoidance of predators,

better finding of prey, and caring for young to promote their survival. Such pressures have acted on the common genetic material inherited from the common ancestral stock. In many cases, the independently achieved results combine some strikingly similar features with some markedly different ones. A notable example of this phenomenon is the evolution of the forebrain, the most rostral part of the brain. Within all four vertebrate radiations, a set of some of the species have independently gained enlarged and more complexly organized forebrains, and these more elaborate forebrains often are correlated with more complex behavioral repertoires.

In our overview of the vertebrate nervous system in Chapter 3, we covered the major regions of the brain and outlined some of the major systems that are common to many species. Within each of the four major vertebrate radiations, marked variation exists in the relative size of various regions involved in these systems and in the elaborateness of nuclei and cortical regions. In some species within each radiation, most neuronal cell bodies remain near the ventricular surface and form relatively few distinct, migrated, individual nuclei or cortical layers. In other species in each radiation, however, extensive migration of the neurons takes place, which results in the formation of complexly structured nuclear groups and, in some cases, elaborately layered cortices. In these latter species, the brains also tend to be larger, relative to body size, than the brains of species with less complexly structured brains. The selective pressures for such larger brains and for increases in behavioral complexity are discussed in detail in Chapter 5.

In this chapter we will first briefly review vertebrate phylogeny. Then we will identify the members of each of the various groups and provide a series of outline drawings of some

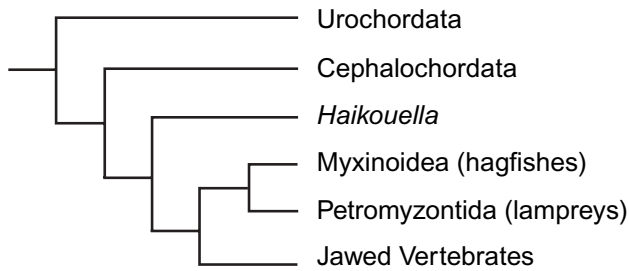


FIGURE 4-1. Cladogram of the chordates showing monophyly of the cyclostomes (hagfishes and lampreys) after Furlong and Holland (2002, see Box 4-1). The vertebrates comprise the cyclostomes, or agnathans—hagfishes and lampreys—and jawed vertebrates, or gnathostomes. The extinct taxon *Haikouella* is included here, since it recently has been recognized from fossil evidence as the sister group of vertebrates [Chen et al. (1999); Mallatt and Chen (2003)].

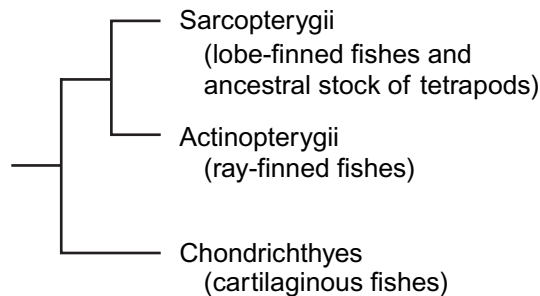


FIGURE 4-2. Cladogram of the gnathostomes. Ancestral Osteichthyes, or bony fishes, gave rise to the actinopterygian and sarcopterygian radiations.

of their brains for future reference. Next we will consider the variation in structural complexity within each major group, recognizing that extant species can be divided into two major types of brain organization. We believe that approaching the study of comparative neuroanatomy by comparing these two major types of brain organization across the four major vertebrate groups can help to provide a clearer picture of the multiple, independent changes that have occurred in brains over the course of evolution.

VERTEBRATE PHYLOGENY

Chordate Relationships

Cephalochordates (*Branchiostoma*) have long been regarded as the most proximal group to the vertebrates. The recent discovery of fossils of the Lower Cambrian (520 million years old) chordate *Haikouella* by Jun-yuan Chen, Jon Mallatt, and their collaborators has changed that viewpoint. As shown in Figure 4-1, *Haikouella* appears to be more closely related to vertebrates than the cephalochordates. *Haikouella* fossils are only a few millimeters in length but exhibit a number of chordate features, including a notochord and a dorsally lying nerve cord. A relatively enlarged brain and paired, lateral eyes are present at the rostral end of the nerve cord. Deuterostome and chordate origins will be considered in more detail in the last chapter of this book, Chapter 31.

Jawless Vertebrates

The term **Agnatha** (a = without; gnathos = jaw), or **cyclostomes**, is used to refer to two groups of extant vertebrates, hagfishes and lampreys (Fig. 4-3). Recent molecular

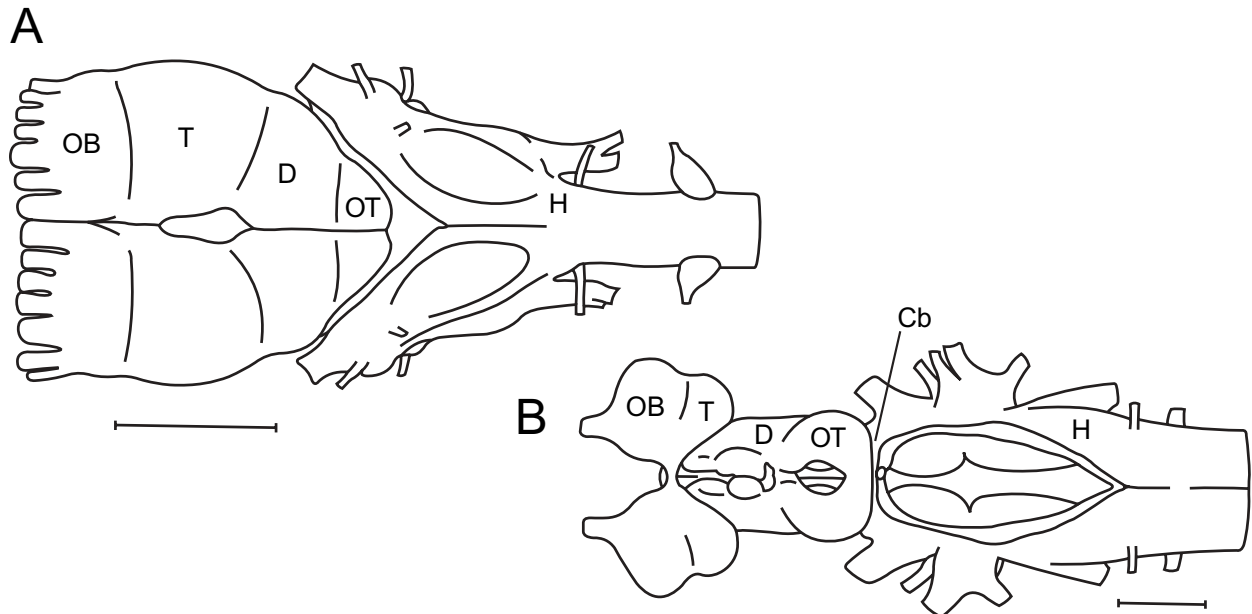


FIGURE 4-3. (A) Dorsal view of the brain of a Pacific hagfish (*Eptatretus stouti*). Scale = 2 mm. Adapted from Wicht and Northcutt (1992). (B) Dorsal view of the brain of a silver lamprey (*Ichthyomyzon unicuspis*). Scale = 1 mm. Adapted from Northcutt and Puzdrowski (1988). Both used with permission of S Karger AG, Basel. Abbreviations used in this and other similar figures in this chapter: Cb, cerebellum; D, diencephalon; H, hindbrain; OB, olfactory bulb; OT, optic tectum; T, telencephalon.

analysis has convincingly demonstrated that, despite recent discussion to the contrary, hagfishes and lampreys are monophyletic and are both bona fide members of the vertebrate clade (see Box 4-1). We thus treat them as members of the cyclostome radiation and the latter as one of the four major vertebrate radiations here.

Jawless vertebrates also include numerous taxa that are extinct. These taxa were a diverse group. Some had heavy, bony shields covering the rostral end of the body, with openings for two, dorsally placed eyes, a pineal eye, and a single, median nostril, as well as a round, jawless mouth with up to 10 pairs of gill slits. Many were bottom dwelling, detritus feeders. One group, the anaspids, lacked heavy shields and were more active swimmers. Some of the differences between the extant hag-

fishes and lampreys reflect this range of diversity. All hagfishes are marine, but while some lampreys are marine, all spawn in freshwater rivers. Lampreys undergo a larval (**ammocoete**) stage followed by a metamorphosis to the adult form. Lampreys are true parasites, which attach to the body surface of other fishes, while hagfishes are scavengers, which feed by entering the body cavities of dead or dying fishes.

An additional group of extinct jawless vertebrates, the **conodonts**, has been identified primarily by comb-like tooth elements for which they are named. Whether they are monophyletic with the cyclostomes is presently undetermined. The conodonts are thought to have had an actively predatory mode of life, which may thus also have characterized the earliest vertebrates.

BOX 4-1. Hagfishes: Invertebrate Chordate or Legitimate Vertebrate?

Rather than placing both hagfishes and lampreys within the single taxon of the cyclostomes, or agnathans, it has been recent practice to separate them. Two radiations of the so-called craniates have been recognized—hagfishes and vertebrates. Hagfishes have been regarded as invertebrate craniates, since they lack true vertebrae, whereas vertebrates have been regarded as including only lampreys and the three radiations of jawed vertebrates. The latest information from molecular analysis contradicts this view, however. In 1998, Jon Mallatt and Jack Sullivan obtained 28S ribosomal DNA sequences from lancelets (*Branchiostoma*), hagfishes (*Eptatretus*), lampreys (*Petromyzon*), and cartilaginous fishes (the chimaera *Hydrolagus* and the spiny dogfish *Squalus*). They compared these sequences with each other and with known sequences from other vertebrate groups. This analysis strongly supported monophyly of cyclostomes and contradicted the recent idea that lampreys are the sister group of jawed vertebrates. Rather, lampreys and hagfishes are sister taxa and together constitute a monophyletic outgroup to jawed vertebrates, as earlier models of phylogeny had posited.

Rebecca Furlong and Peter Holland carried out a similar study more recently and reached the same conclusion. They analyzed three types of genes—18S ribosomal DNA, mitochondrial genes, and nuclear protein-coding DNA—and found strong support for placing hagfishes and lampreys together in a monophyletic cyclostome clade. Their findings and perspective are summarized here. The three types of genes were analyzed independently, since they differ in several dimensions, including their mode of inheritance and rate of evolution. In the nuclear protein-coding category, two different genes were analyzed, thus providing a total of four data sets altogether. These data sets each supported the same conclusion of monophyly for hagfishes and lampreys and with high statistical probabilities for three of the four genes. From this analysis, Furlong and Holland concluded that the probability of cyclostome monophyly is much higher than the alternative scenario of lampreys and

gnathostomes being sister taxa with hagfishes as their outgroup.

Hagfishes and lampreys have a number of shared features, which are therefore likely to be homologues. These features include the lack of jaws, lack of dermal armour, presence of a single, median nostril, a circular mouth, and pouch-like gills. They also exhibit many differences, including the lack of true vertebrae in hagfishes. Other features that hagfish lack but are shared by lampreys and jawed vertebrates, in addition to the presence of true vertebrae, include the presence of radial muscles in the fins, a lateral line system, and extraocular eye muscles and their respective cranial nerves. As Furlong and Holland discussed, these features may have been independently evolved in lampreys and jawed vertebrates or, as they think more likely, may have been present in the common vertebrate ancestor and secondarily lost in hagfishes.

The findings of these studies contradict the phylogenetic tree that separates hagfishes from lampreys and designates them as invertebrate craniates while lumping lampreys and gnathostomes as “vertebrates.” Furlong and Holland regard the terms craniate and vertebrate as synonymous but favor use of the better known term vertebrate for the clade of both cyclostomes and gnathostomes. Just as snakes are regarded as tetrapods, having secondarily lost their limbs, so may hagfish be regarded as vertebrates, having secondarily lost true vertebrae. We thus also use the term vertebrate, rather than craniate, for cyclostomes and gnathostomes in this book.

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Chondrichthyes

Cartilaginous fishes (Chondrichthyes) comprise two major groups: **Holocephali** and **Elasmobranchi** (Fig. 4-4). None of the cartilaginous fishes are known to have a larval stage. The **Holocephali** are the chimaeras [Fig. 4-5(A)], or ratfishes, and are distinctive in appearance with large eyes and tapering, thin tails. The elasmobranchs are the sharks, skates, and rays. Squalomorph sharks include hexanchids [cow sharks, Fig. 4-5(B)], squaliform sharks [such as the spiny dogfish shark, Fig. 4-5(C)], and pristiphoriform (saw) sharks. Squatinomorph sharks (angel sharks, or monkfish) have flattened bodies similar to rays but swim like other sharks by using their bodies and tails. Galeomorph sharks include bullhead, carpet, mackerel, and requiem sharks. The mackerel sharks (Family Lamnidae) include the giant white shark (or man-eater), as well as mako and basking sharks. Most of the Batoidea are characterized by their flattened bodies. They include skates [Fig. 4-5(D)], sawfishes, guitarfishes, electric rays, stingrays, eagle rays, and manta rays.

Actinopterygii

The Actinopterygii comprise five radiations of **ray-finned fishes** (Fig. 4-6). Ray-finned fishes are one of the most widely distributed radiations of vertebrates. They inhabit Arctic to tropical waters, deep sea depths to surface waters to a partially air habitat, and both fresh and salt water. **Cladistia**, the bichirs and roperfishes (Fig. 4-7), both also called reedfishes, are elongated in shape and live in shallow, tropical rivers and swamps. **Chondrostei** include sturgeons, some of which can reach a length of 4m and weigh over 500kg, and the smaller paddlefishes (or spoonbills). **Ginglymodi**, the gars [Fig. 4-8(A)], are distinguished by their elongated snouts and bodies. **Halecomorphi** have only one extant species, the bowfin *Amia calva* [Fig. 4-8(B)]. Reedfishes, sturgeons, paddlefishes, gars, and the bowfin all have skeletons that are largely cartilaginous. Highly vascularized air bladders can be used as auxiliary lungs for

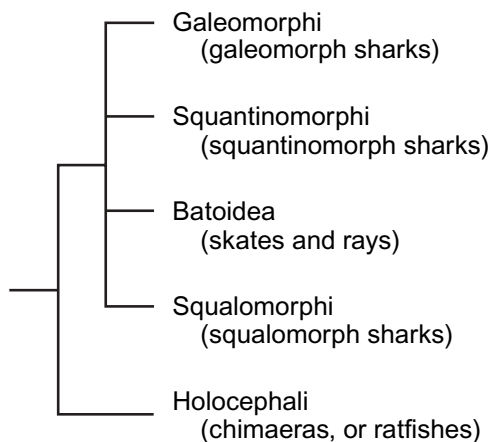


FIGURE 4-4. Cladogram of the cartilaginous fishes. Ancestral Chondrichthyes, or cartilaginous fishes, gave rise to the Holocephali and to Elasmobranchs, which comprise the rest of the cartilaginous fishes, the sharks, skates, and rays.

short periods of time, but no species in these groups is known to undergo a larval stage and metamorphosis. The fifth group of ray-finned fishes, the **teleostei**, differs from other ray-finned fishes in having bony skeletons and in their vast number and diversity of species. Larval stages followed by metamorphosis have been found in a number of teleost taxa. The group that comprises the ginglymodi (gars), halecomorphi (bowfin), and teleosts are referred to as **neopterygii**.

Teleosts comprise four major groups (Fig. 4-9). Caution must be noted, however, that not all these groups, or some of the taxa within them, can be assumed to be monophyletic. Additional study is needed to clarify a number of relationships within this extremely large and diverse radiation. **Osteoglossomorphs** include arawanas, arapaimas, mooneyes, and the freshwater butterfly fish, all of which have relatively large eyes and live in fresh water; notopterids (also known as featherbacks or knifefishes), which have exceptionally long anal fins; and mormyrids, which are weakly electric. **Elopomorphs** are all saltwater fishes; they include tarpons, bonefishes, and eels. **Clupeomorphs** include herrings, anchovies, menhadens, shad, and aelwives. Many species of clupeomorph fishes form huge schools. Both elopomorphs and clupeomorphs possess metamorphosing species. **Euteleostei** (Fig. 4-10) include the great majority of the more than 20,000 teleost species and comprise over 25 orders, 375 families, and 17,000 species.

Euteleosts include a number of diverse and familiar species, such as pikes, goldfishes, salmon, cods, and livebearers, in addition to their largest group, the percomorphs. Percomorphs include equally diverse species, including tunas, dories, stone fishes, porcupine fishes, flounders and soles, flying gunards, sea horses, perches, sunfishes, cichlids, snappers, and many others. Members of this diverse group occupy a great variety of niches. Some species have larval stages. Some are voracious predators. A number, particularly those that inhabit coral reefs, have complex and elaborate territorial displays and courtship rituals, pair bonding, and biparental care of young. Those with the most complex repertoires also exhibit the most complex and enlarged brains.

Most studies on the central nervous system of fishes have been carried out on elasmobranchs and actinopterygians. A relatively few number of studies have been done on hagfishes and lampreys, and more are needed on these two important cyclostome taxa. Relatively little information is available on holocephalians, and most studies on actinopterygians have focused on euteleosts.

Sarcopterygii

The sarcopterygian radiation of fleshy-finned fishes and tetrapod vertebrates (Fig. 4-11) is the large, sister radiation of the Actinopterygii. Three extant groups—**Dipnoi**, **Actinistia**, and **Tetrapoda**—are descended from the ancestral sarcopterygian stock. As is the case with ray-finned fishes, this radiation is widely distributed, with habitats ranging from the Arctic to the tropics; it includes fishes, amphibians, and land vertebrates. Actinistia are represented by only one extant species, the **coelacanth** (or **crossopterygian**), *Latimeria chalumnae* [Fig. 4-12(A)]. Specimens of this fish were first taken from deep waters off the South African coast in the 1930s. They are regarded as “living fossils,” as their skeletal form

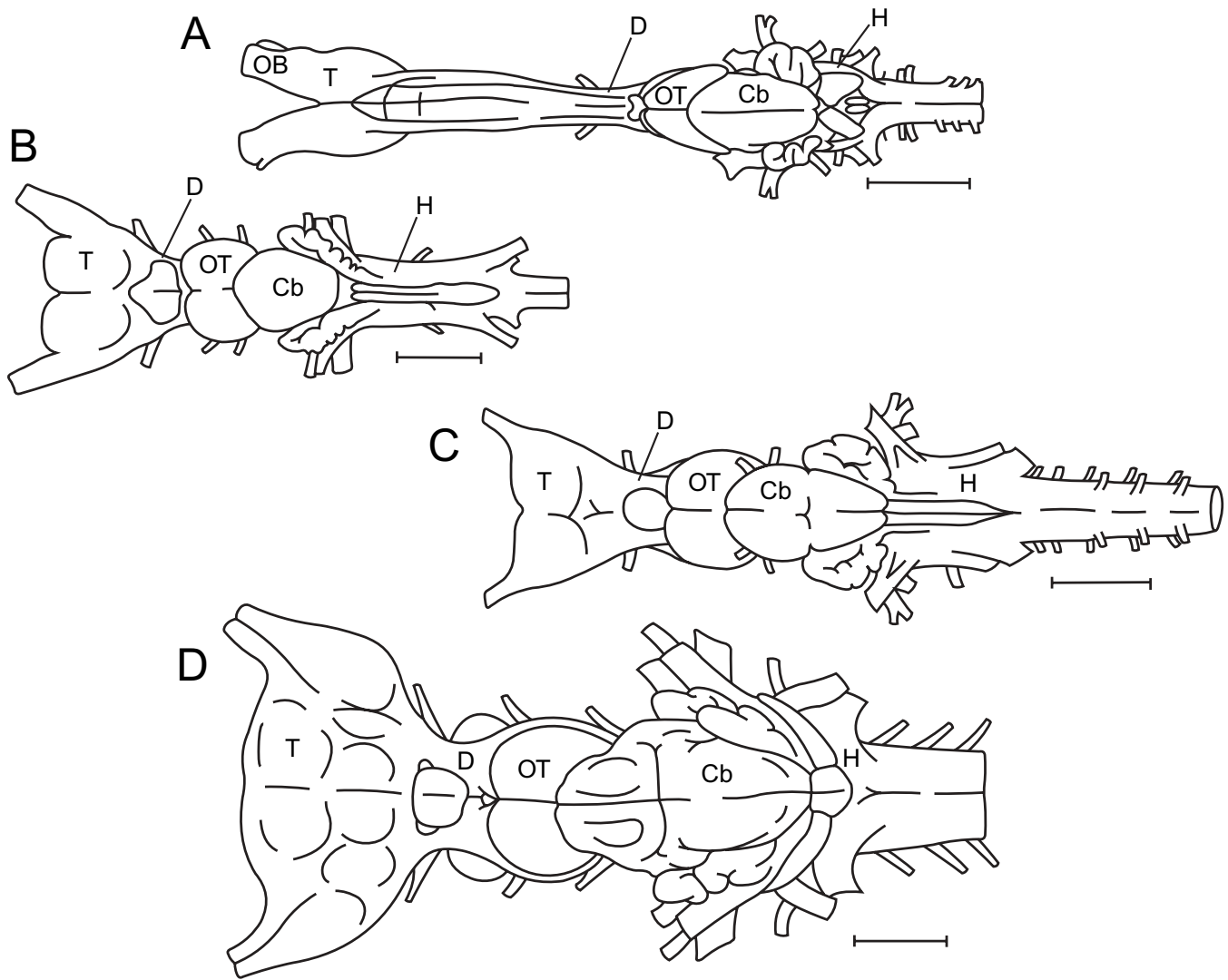


FIGURE 4-5. (A) Dorsal view of the brain of a chimaera (*Hydrolagus coliei*). Scale = 1 cm. Adapted from Northcutt (1978). (B) Dorsal view of the brain of a cow shark (*Notorynchus maculatus*). Scale = 1 cm. Adapted from Northcutt (1978). Note that for this and most other species illustrated in this chapter in which the olfactory bulbs are at the distal ends of elongated olfactory tracts, only the proximal stump of the olfactory tract is shown. (C) Dorsal view of the brain of a spiny dogfish shark (*Squalus acanthias*). Scale = 1 cm. Adapted from Northcutt (1979). Used with permission of The University of Chicago Press. (D) Dorsal view of the brain of the clearnose skate (*Raja eglanteria*). Scale = 5 mm. Adapted from Northcutt (1979). Used with permission of The University of Chicago Press.

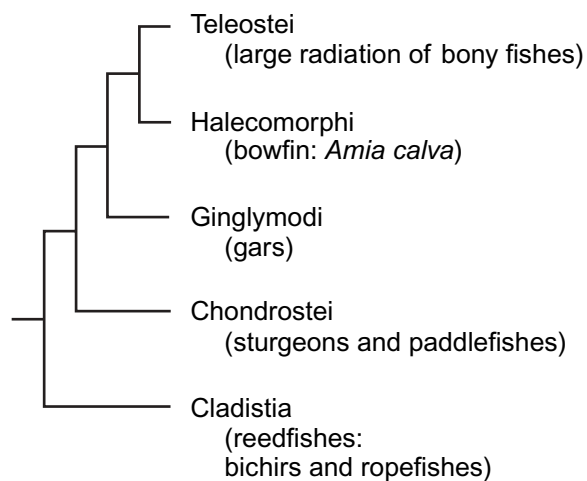


FIGURE 4-6. Cladogram of the ray-finned fishes, or Actinopterygii.

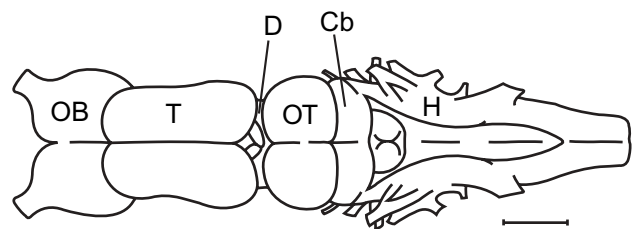


FIGURE 4-7. Dorsal view of the brain of a bichir (*Polypterus palmas*). Scale = 2 mm. Adapted from Reiner and Northcutt (1992) and used with permission of John Wiley & Sons.

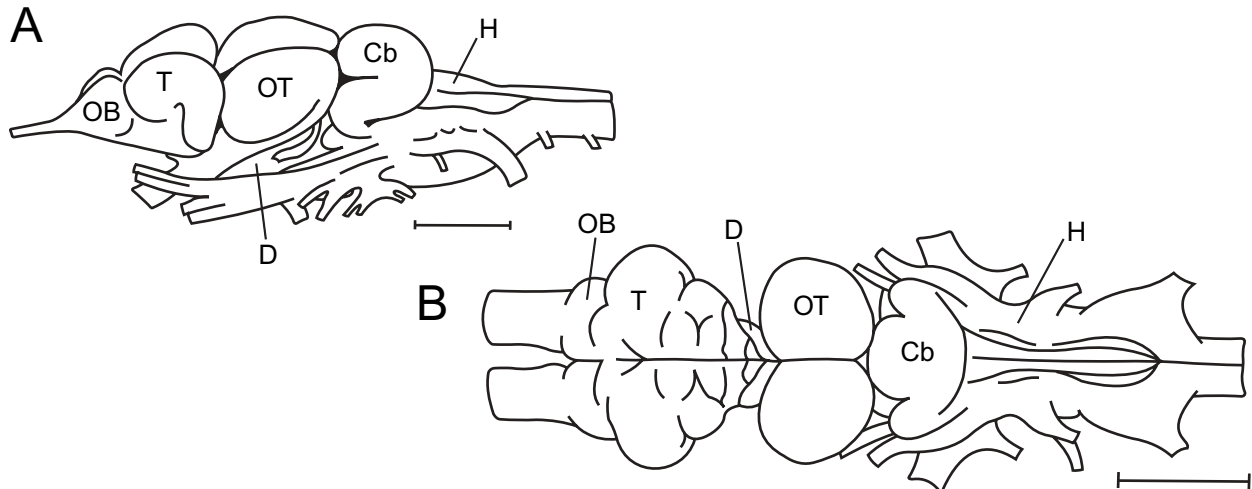


FIGURE 4-8. (A) Lateral view of the brain of a longnose gar (*Lepisosteus osseus*). Scale = 3 mm. Adapted from Northcutt and Butler (1976). (B) Dorsal view of the brain of a bowfin (*Amia calva*). Scale = 5 mm. Adapted from Butler and Northcutt (1992). Used with permission of S. Karger AG, Basel.

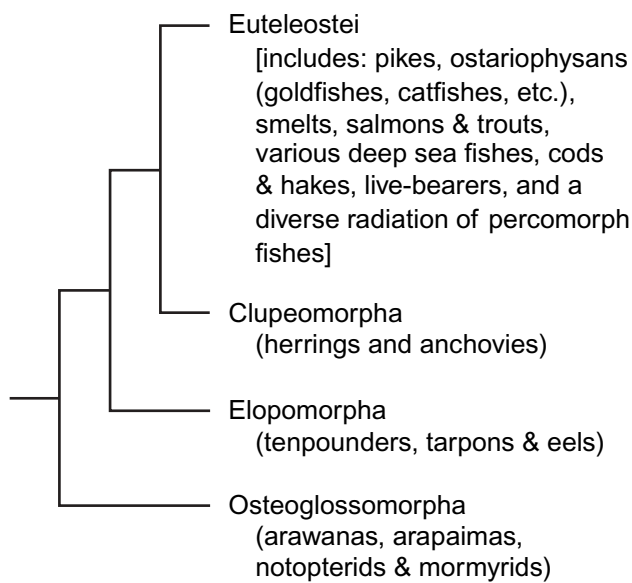


FIGURE 4-9. Caldogram of the teleost fishes.

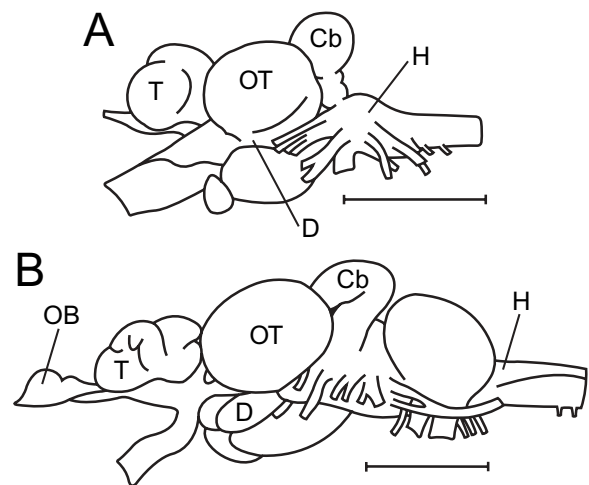


FIGURE 4-10. Lateral views of the brains of (A) a sunfish (*Lepomis cyanellus*) and (B) a goldfish (*Carassius auratus*). Scales = 5 mm. Adapted from Northcutt and Butler (1991) and Northcutt (1983), respectively, and used with permission of S. Karger AG, Basel and The University of Michigan Press.

has not changed since the Devonian period (over 300 million years ago). Studies comparing the sequences of amino acids in hemoglobin chains indicate that *Latimeria* is more closely related to amphibians than to any other fish. Thus, coelacanth appears to be the sister group of tetrapods.

Dipnoi, the lungfishes [Fig. 4-12(B)], are also similar to species identified from the Devonian. Their air bladder is highly vascularized and enables these tropical, freshwater fishes to survive out of water if moisture is maintained on the skin. Neither coelacanth nor lungfishes undergo metamorphosis. Specimens of *Latimeria* are particularly rare, but some information on the organization of its brain is available. The brain is

very similar in structure to that of some of the lungfish, on which more studies have been done.

Extant tetrapods comprise amphibians and amniotes, or land vertebrates. Amphibians arose in the Devonian period and include **gymnophionans** (**caecilians**: worm-like burrowers with minute eyes and persistent notochord), **urodeles** [newts and salamanders, Fig. 4-12(C)], and **anurans** [frogs and toads, Fig. 4-12(D)]. Whether amphibians are monophyletic or polyphyletic remains unresolved, however. In some amphibians, particularly salamanders, the skeleton is partially cartilaginous. Most amphibians have a larval stage and undergo metamorphosis, but some salamanders (*Necturus*, the mudpuppy)

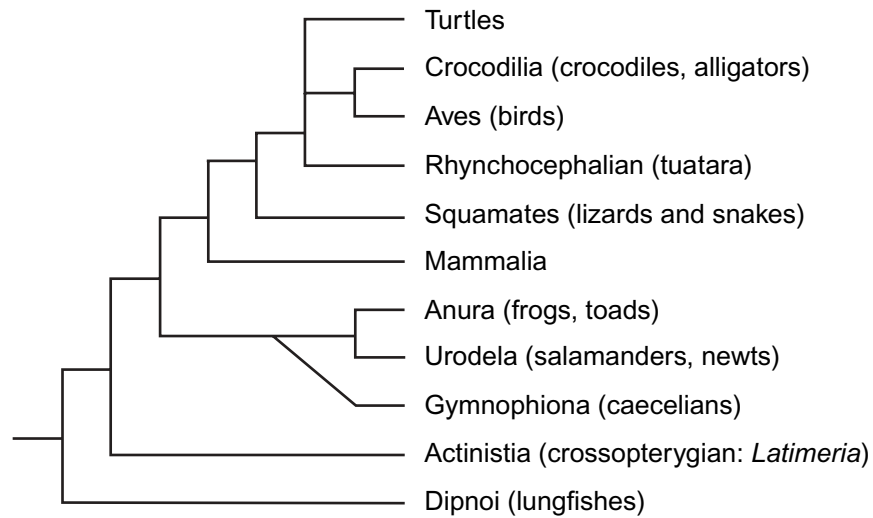


FIGURE 4-11. Cladogram of the sarcopterygian radiation. Ancestral sarcopterygians gave rise to the lungfishes, the crossopterygian fish *Latimeria*, and the tetrapods, which include the amphibians and amniotes. The amniotes can now be classified as either synapsids, of which extant forms comprise the mammals, and diapsids, which include turtles, crocodiles, and birds, and the tuatara, and, as a sister group to all the latter, the squamates, lizards, and snakes.

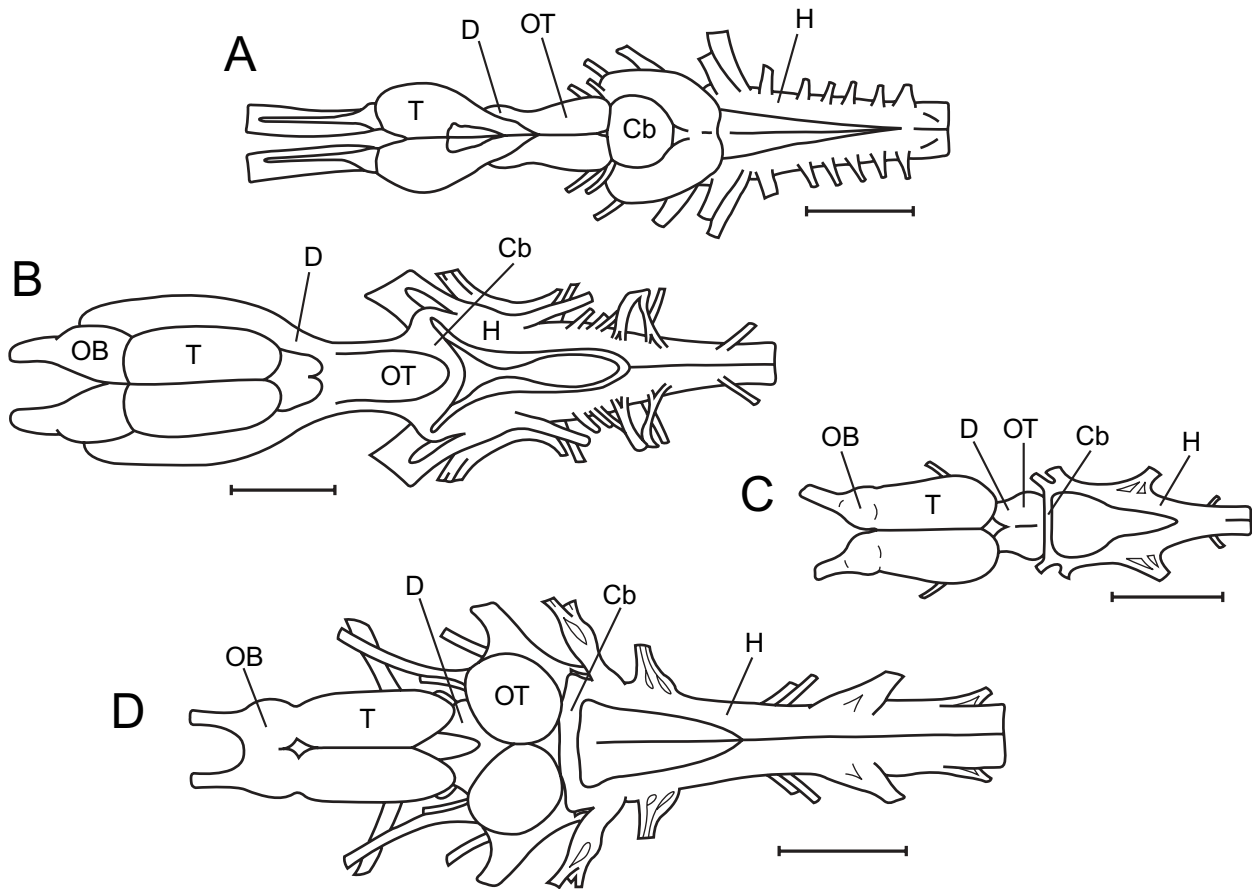


FIGURE 4-12. (A) Dorsal view of the brain of a coelacanth (*Latimeria chalumnae*). Scale = 1 cm. Adapted from Northcutt et al. (1978). (B) Dorsal view of the brain of an African lungfish (*Protopterus annectens*). Scale = 5 mm. Adapted from Northcutt (1977). (C) Dorsal view of the brain of a mudpuppy (*Necturus maculosus*). Scale = approximately 3 mm. Adapted from Northcutt (1979). Used with permission of The University of Chicago Press. (D) Dorsal view of the brain of a bullfrog (*Rana catesbeiana*). Scale = 10 mm. Adapted from Northcutt and Royce (1975). A, B, and D used with permission of John Wiley & Sons.

retain the larval stage throughout their life cycle. Many caecilians are viviparous.

A limited amount of data is available on the brain of lungfishes, and more research is needed on this important group. Very few studies have been done on *Latimeria* due to its extreme rarity. Most studies of the central nervous system in amphibians have been done on anurans; some data are available on urodeles, but data on the central nervous system of caecilians are very limited.

Extant amniotes (Fig. 4-11) comprise mammals, reptiles, and birds. The term reptiles is used to refer to extant lizards, snakes, tuatara, crocodiles, and turtles, even though these animals do not form a biologically unitary group. A phylogenetically more correct use of the term reptiles that has not yet been adopted in general usage would be to include birds in its purview. Nonetheless, we will use the word reptile in its usual sense throughout this book, applying it to lizards, snakes, tuatara, crocodiles, and turtles.

The earliest amniotes had **anapsid** skulls, i.e., they lacked any fenestrae in the skulls. Fenestrae are openings formed by bony arches that occur in the lateral, or temporal, part of the skull. Rather than being bowed out over the outer surface of the skull, muscles that pass through them and insert on the jaw can contract in a straight line, resulting in a more powerful bite. The first taxon that diverged from the ancestral amniote stock were **synapsid** amniotes (see Box 4-2), which ultimately gave rise to mammals. The term synapsid refers to the presence of one, laterally placed temporal fenestra.

In contrast to the synapsid condition, **diapsid** skulls have two temporal fenestrae and two bony arches in the skull. Lizards, snakes, the tuatara, crocodiles, and birds are classified as diapsids. The true diapsid condition is retained in the tuatara and in crocodiles, but it has been modified secondarily in the other diapsid taxa. Lizards lack the bony arch ventral to the lower opening, snakes additionally lack the bony arch separating the two openings, and birds have a single, fused temporal opening that also has continuity with the orbit. Turtles have anapsid skulls, which are characterized by a complete roof of bone in the temporal region, lacking any fenestrae or arches. Since the earliest ancestral amniotes also had anapsid skulls, turtles were thought to have diverged from them independently of the diapsid and synapsid lines. Recent evidence, however, strongly supports the grouping of turtles with other reptiles and within the diapsid lineage. They have secondarily modified their skulls, losing both temporal fenestrae (see Box 4-3).

Mammals comprise three major groups (Fig. 4-13)—Prototheria, Metatheria, and Eutheria. **Prototheria**, the **monotremes**, reproduce by laying eggs. They have pouches and mammary glands without nipples. Monotremes consist of the platypus and echidnas, or spiny anteaters (Fig. 4-14). **Metatheria**, the marsupials, are viviparous but lack a typical placenta. After birth, the embryos crawl into a skin pouch where they complete their development.

Eutherian mammals (Figs. 4-13, 4-15, and 4-16) are viviparous and are those mammals in which embryological development occurs within a placenta formed by the apposition of the uterine lining and the extraembryonic membranes of the embryo. Eutheria are a diverse radiation, occupying niches in the ocean (cetaceans) and partially in the air (bats)

as well as on land. Specializations of the limbs and/or their distal portions, such as hooves and hoof-like structures in artiodactyls (pigs, camels, cows, etc.) and perissodactyls (rhinos, horses, etc.), opposing digits in primates, wing-like membranes in bats, and reduction in cetaceans and seals, are common. Specializations related to prey capture and consumption, such as the dentition in carnivores and rodents, elongation of the snout in edentates, pangolins, and elephants, and tool making in primates are also diverse and pronounced.

As is the case with other vertebrate groups, the phylogenetic relationships of mammals (including those illustrated here) are still subject to revision as new data become available, particularly in genetic sequencing studies. The cladogram shown in Figure 4-13 indicates a close relationship of primates to rodents and rabbits relative to other mammalian taxa. Also note that moles, shrews, and hedgehogs are listed as Eulipotyphla; these are commonly known as insectivores. While at least some aspects of central nervous system organization have been studied in a number of mammalian species—including monotremes, marsupials, and a number of species of placental mammals—most mammalian studies have focused on the more common placental mammals, such as rodents, domestic cats, and macaque monkeys.

Extant diapsids comprise two groups (Fig. 4-11), one of which is the **Squamata**, the lizards and snakes. The other group includes the **Rhynchocephalia**, the lizard-like tuatara (genus *Sphenodon*) native to New Zealand, turtles (see Box 4-3), and the **Thecodontia**, or **Archosauria**, which comprises crocodiles (**Crocodylia**) and birds (**Aves**). Among the diapsids, birds [Figs. 4-17, 18(A)] comprise a large radiation of 8,700 species (compared with 6,000 species of reptiles and 4,500 species of mammals). Turtles [Fig. 4-18(B)] comprise four major groups: leatherback sea turtles, true sea turtles, side-necked turtles, and hidden-necked turtles.

Birds are uniquely characterized by feathers. Their bones are filled with hollow spaces for lightness, metacarpals are fused, and teeth are absent. Numerous variations in size, habitat, structure of bill, and courtship and brooding behaviors exist. The largest group is the Passeriformes, which are perching birds, such as the sparrows, and include over 5,000 species. Other groups with between 250 and 400 species each are the Apodiformes (swifts and hummingbirds), Piciformes (including woodpeckers and toucans), Falconiformes (eagles, hawks, and vultures), Galliformes (gallinaceous, chicken-like birds), Charadriiformes (shorebirds and gulls), Columbiformes (pigeons and doves), and Psittaciformes (parrots). Smaller orders include penguins, rheas, ostrich (a single species), emus, kiwis, tinamous, grebes, albatrosses and petrels, pelicans and comorants, herons and flamingos, waterfowl, cranes, loons, cuckoos, owls, nightjars, mousebirds, trogons, and kingfishers.

Among reptiles, a fair sampling of species has been achieved in the study of central nervous system organization. Despite the great range of variation among extant species of birds, most studies of central nervous system organization in birds have been done on pigeons (Columbiformes) and owls (Strigiformes). A number of studies on songbirds have also been done that explore relationships among learning, reproductive functions, and the development of parts of the brain involved in song production. Over the past quarter century, our concepts of brain organization in these groups of nonmammalian

BOX 4-2. The Early Divergence of Synapsids

An idea that is common among newcomers to the field of vertebrate evolution is that the earliest mammals evolved from reptile ancestors. This idea can lead to summary statements of tetrapod phylogeny as being something along the lines of *amphibians-reptiles-birds and mammals*. Unfortunately, this sequence is not consistent with current data about the times of divergence of various tetrapod lineages. Reptiles, which are diapsids (having two temporal fenestrae, as discussed above), did not appear in the fossil record until 10 million years after the origin of the line leading to modern mammals.

As shown in Figure 1, approximately 350 million years ago, the stem tetrapods split into two lines, one leading to modern amphibians and a second line that became the stem

anapsids, which were the ancestors of the amniotes. 320 million years ago, the stem synapsids branched from the anapsid line. Figure 2 (top) shows the skull of an anapsid, with no temporal opening, and the skull of a synapsid (middle) with a single temporal opening, shown in dark gray. As indicated in Figure 1, the synapsids eventually led to the emergence of mammals.

Ten million years after the appearance of the first synapsids, the anapsid lineage diverged again into two lines of diapsids, as shown in Figure 2 (bottom). Thus, the stem diapsids produced one branch that led to the modern lizards and snakes and a second branch that led to crocodiles and birds, turtles, and tuataras. Although some controversy exists about the exact location of the turtle branch of this

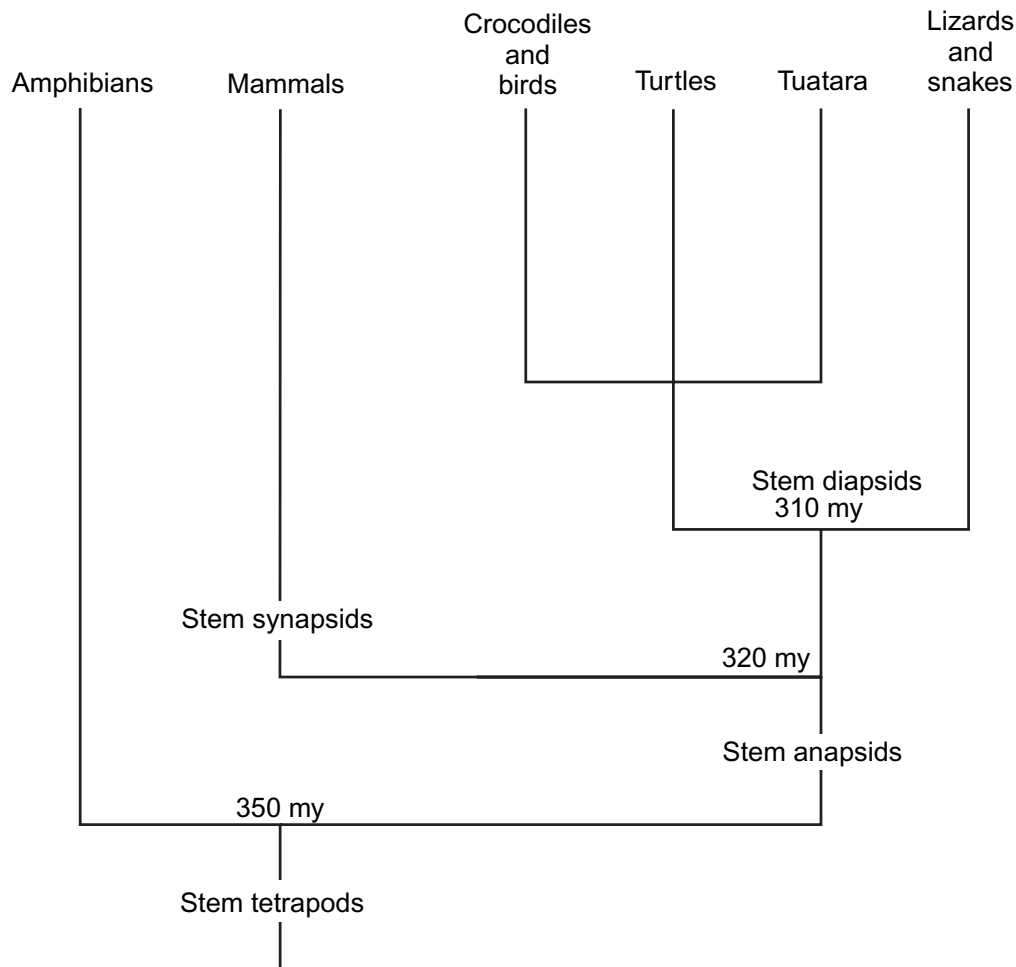


FIGURE 1. A cladogram of tetrapod evolution. The stem synapsids, which led to modern mammals, split off from the stem anapsids approximately 10 million years before the appearance of the stem diapsids, which led to modern reptiles and birds. Adapted from Evans (2000).

BOX 4-2. The Early Divergence of Synapsids—cont'd

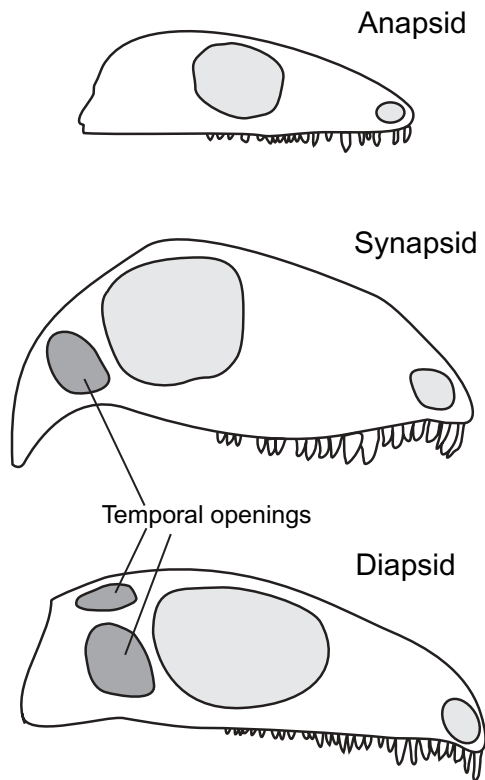


FIGURE 2. Skulls of early amniotes showing the temporal openings (darker grey areas) that characterize them: anapsid (no opening), synapsid (one opening), and diapsid (two openings). The large, light gray circular areas in each skull are the orbits, which contained the eyes, and the smaller, light gray circular areas are the nares. Adapted from Carroll (1988) and used with permission of Henry Holt & Company.

genealogical tree, the early divergence of the stem synapsids, which led to the modern mammals, is not in dispute.

As Figure 1 indicates, the correct temporal sequence of tetrapod evolution is *amphibians-mammals-reptiles and birds*.

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BOX 4-3. Turtles: Welcome Home to Diapsid-ville!

The phylogenetic relationship of turtles to the rest of the amniotes has long been uncertain. Traditionally, turtles have been treated as one of three major radiations of amniotes, due to multiple characters, the main one of which is the lack of any temporal fenestration in their skulls. Thus, extant amniotes have been grouped into the synapsid radiation of mammals, the diapsids, which include lizards, snakes, the tuatara, crocodiles, and birds, and the anapsid radiation of turtles. Recent evidence from both morphological and molecular studies now strongly supports a revision of this view. Turtles are most closely related to crocodiles and birds and are more closely related to them than lizards and other overtly diapsid reptiles are. There is still debate as to whether turtles or birds are more closely related to crocodiles. In Figure 4-11, crocodiles and birds are grouped most closely with turtles placed as their sister group, based on the molecular evidence of Zardoya and Meyer (2001). Whatever the details of the bird-crocodile-turtle relationships, turtles are clearly descended from the ancestral diapsid stock and have secondarily modified their skulls to lose the temporal fenestrae.

A second modification to the traditional view is to place the tuatara *Sphenodon* as more closely related to birds, crocodiles, and turtles than to the squamates, lizards, and snakes. This relationship is supported by the molecular evi-

dence of Hedges and Poling (1999). The squamates comprise the outgroup to the rest of the diapsid radiation.

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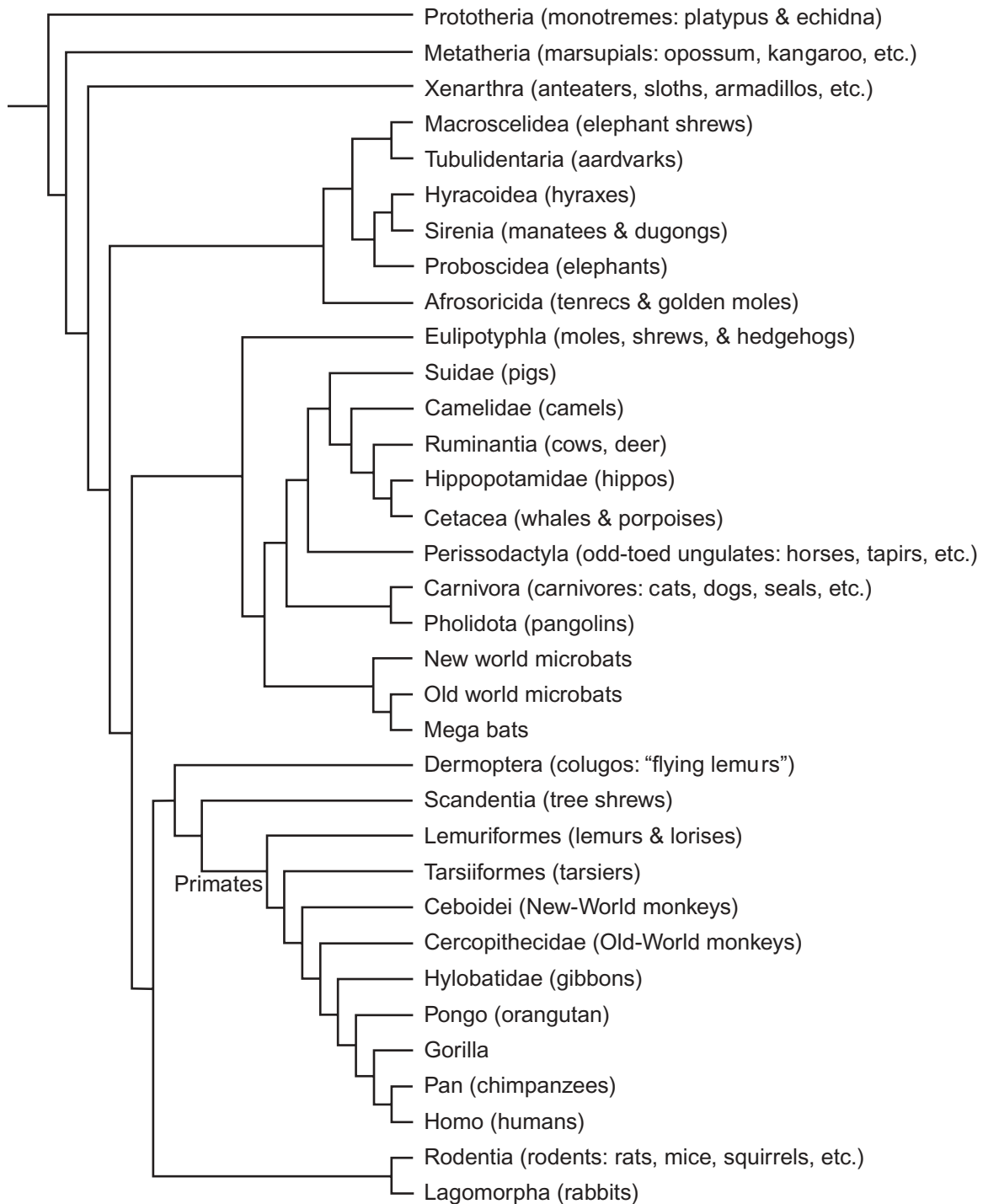


FIGURE 4-13. Cladogram of the mammals. Partially adapted from Kaas and Preuss (2003) and Springer and deJong (2001), as based on Liu et al. (2001).

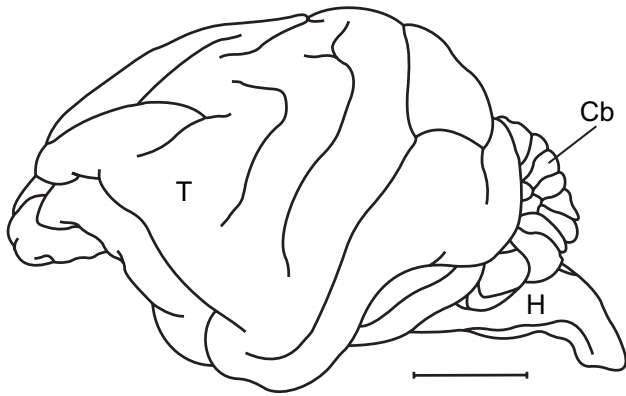


FIGURE 4-14. Lateral view of the brain of an echidna (*Tachyglossus aculeatus*). Scale = approximately 1 cm. Adapted from Rowe (1990). The olfactory bulb, diencephalon, and optic tectum are concealed by the large telencephalon. Used with kind permission of Springer Science and Business Media.

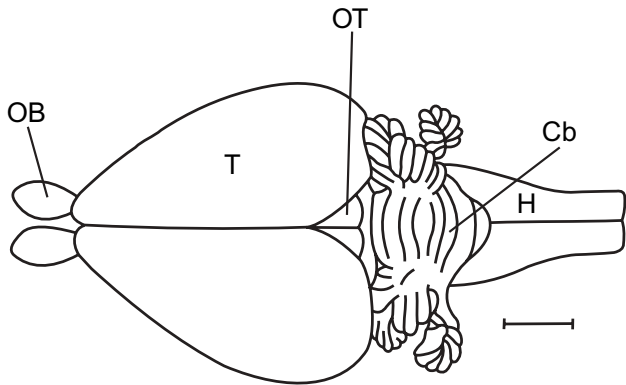


FIGURE 4-15. Dorsal view of the brain of a rabbit (*Lepus sp.*). Scale = approximately 5 mm. Adapted from Northcutt (1979). The diencephalon is concealed by the large telencephalon. Used with permission of The University of Chicago Press.

amniotes, particularly relating to the evolution of sensory systems and forebrain organization, has been extensively reassessed vis-à-vis the organization of the brain in mammals.

The Big Picture of Vertebrate Evolution

Cladograms are typically drawn in a horizontal format, with the species names listed in a vertical array, as shown in this chapter. An alternative presentation is to draw the cladogram vertically, with the species listed horizontally across the top, as in Box 4-2. Figure 4-19, which is a cladogram that shows the descent of the major vertebrate taxa, is presented in yet a third format, one that is not commonly used. This format attempts to dispel erroneous notions prevalent among those with little or no knowledge of paleontology that biological taxa *ascended* a scale, or hierarchy of form, with mammals (and humans in particular) at the top and that evolutionary history

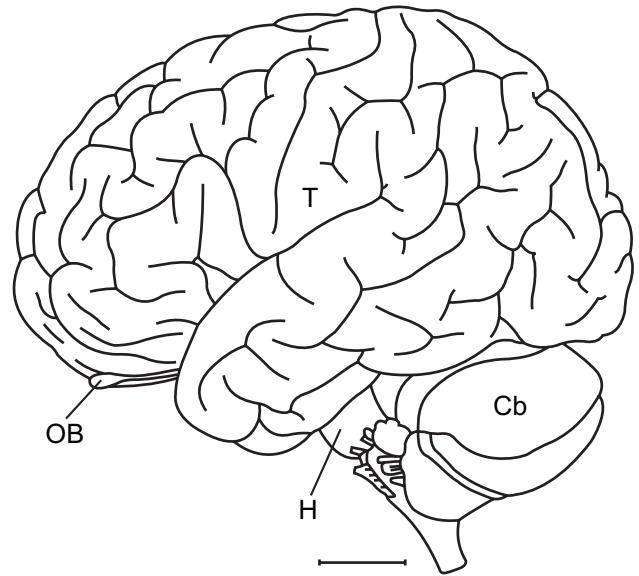


FIGURE 4-16. Lateral view of the brain of a primate (*Homo sapiens*). Scale = 2 cm. Adapted from Nieuwenhuys et al. (1978). The diencephalon and optic tectum are concealed by the large telencephalon. Used with kind permission of Springer Science and Business Media.

followed a sequence something like fish-to-frog-to-reptile-to-bird-to-mammal (see Chapters 1 and 5). Even the most seasoned biologist, from time to time, sometimes thinks in terms of “ascending” a phylogenetic scale, which the typical cladogram format does nothing to impede.

The model of vertebrate evolution presented in Figure 4-19 as a series of staircases arrayed in different directions from the top is intended to show the radiation of vertebrate taxa that are *descended* from a common ancestral stock. It is intended to reinforce the point that there is nothing special about any particular group of descendants, such as mammals or humans, in the overall scheme of evolution; each extant group is as well adapted to its unique environment as the other taxa are to theirs.

TWO TYPES OF BRAIN ORGANIZATION

Within each of the four major radiations of vertebrates—agnathans (or cyclostomes), chondrichthians, actinopterygians, and sarcopterygians—two types of organization may be found in the brains of the various species. We will define the first type as those species in which the brains are characterized by the neuronal cell bodies being unmigrated or only partially migrated away from the embryonic, periventricular matrix, which is the zone from which neurons develop. Afferent projections to these neurons terminate on the more distal portions of their dendrites near the surface of the brain. This pattern of organization will be referred to as **laminar**, in reference to the periventricular lamina in which the majority of neuronal cell

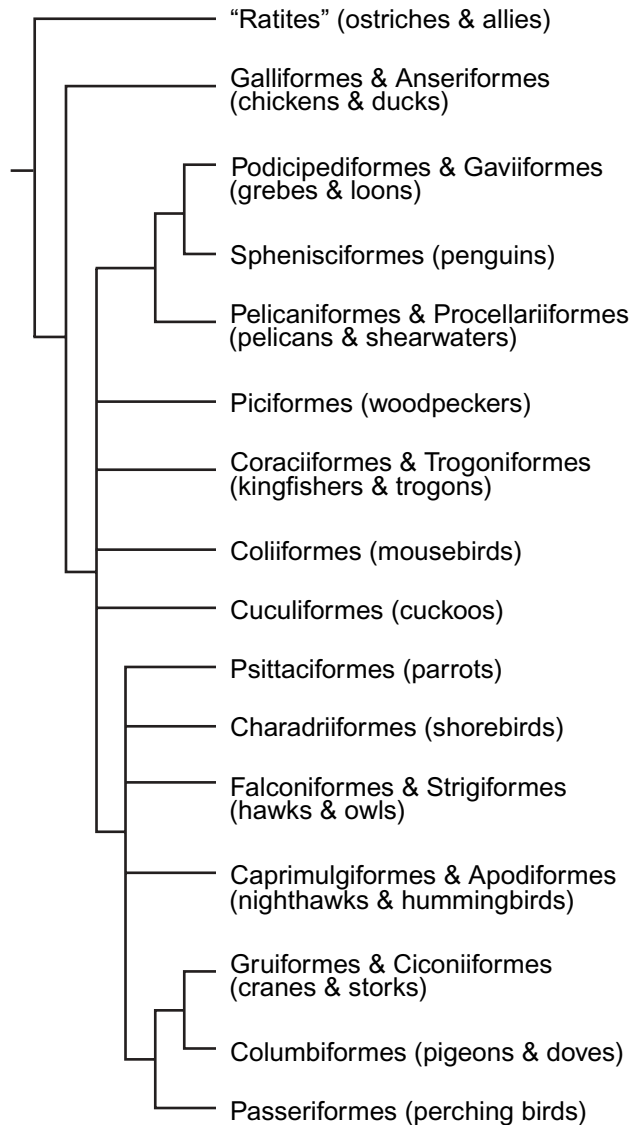


FIGURE 4-17. Cladogram of the birds. Adapted from Liem et al. (2001).

bodies are located. We will refer to the species, from all major radiations, with laminar brains as **Group I**. An example of the arrangement of the neuronal cell bodies within a representative slice of the brain in an animal with a laminar brain is shown in Figure 4-20.

Within each of these various radiations, other species have brains in which extensive migration of neuronal cell bodies away from the periventricular matrix has occurred. More individual nuclear groups are apparent, and the brains are generally relatively larger in size compared with brains exhibiting laminar organization. The pattern of organization in brains with migration of the majority of neuronal cell bodies will be referred to as **elaborated**. Species with elaborated brains will be referred to as **Group II**. An example of the arrangement of

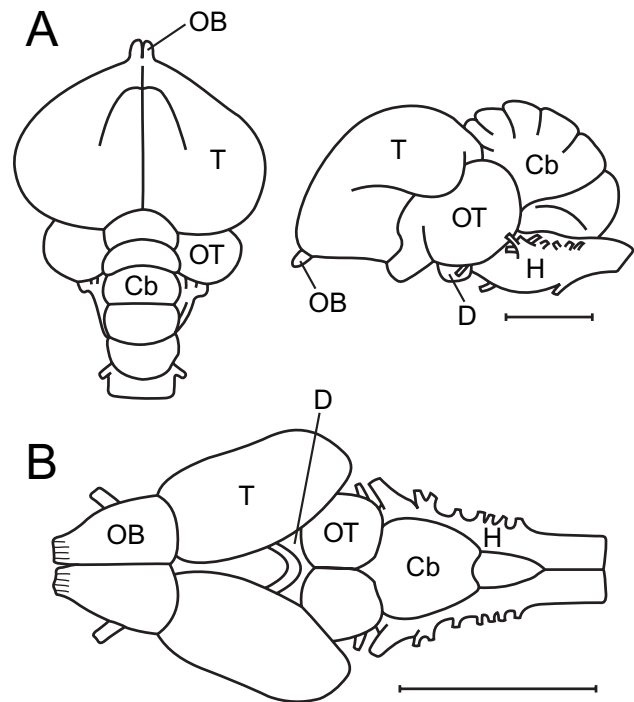


FIGURE 4-18. (A) Dorsal view (left) and lateral view (right) of the brain of a bird (*Columba livia*). Scale = 5 mm. Adapted from Northcutt (1979). (B) Dorsal view of the brain of a turtle (*Chrysemys picta*). Scale = approximately 5 mm. Adapted from Northcutt (1979). Both used with permission of The University of Chicago Press.

the neuronal cell bodies in the brain of an animal with an elaborated brain is shown in Figure 4-21.

The differences in brain organization between Group I and Group II animals are not as notable in the spinal cord and the cranial nerves as in the brain itself. The organization of the spinal cord and cranial nerves is relatively very conservative among all vertebrate radiations, and variation in these structures is more related to habitat (aquatic vs. terrestrial vs. aerial) than to the type of organization of the brain itself. The types of laminar and elaborated brain organization are clearly different in the hindbrain, in the midbrain, and, most prominently, in the forebrain, however. Thus, in a number of the sections on the various regions and systems, we will consider these two major types of organization separately.

The distinction between Group I and Group II is useful for emphasizing the concept that diversity has been achieved independently in different radiations. It is not meant to imply, however, that all brains with either a laminar or an elaborated pattern necessarily will have particular specializations in common. Some features may be distributed in some but not all taxa with laminar brains and also be in some but not all taxa with elaborated brains. Other features may occur in only one or two taxa. Thus, at the end of many sections in the second half of the book (Chapters 15–31), we will summarize the distribution of the various features. Based on that distribution, we

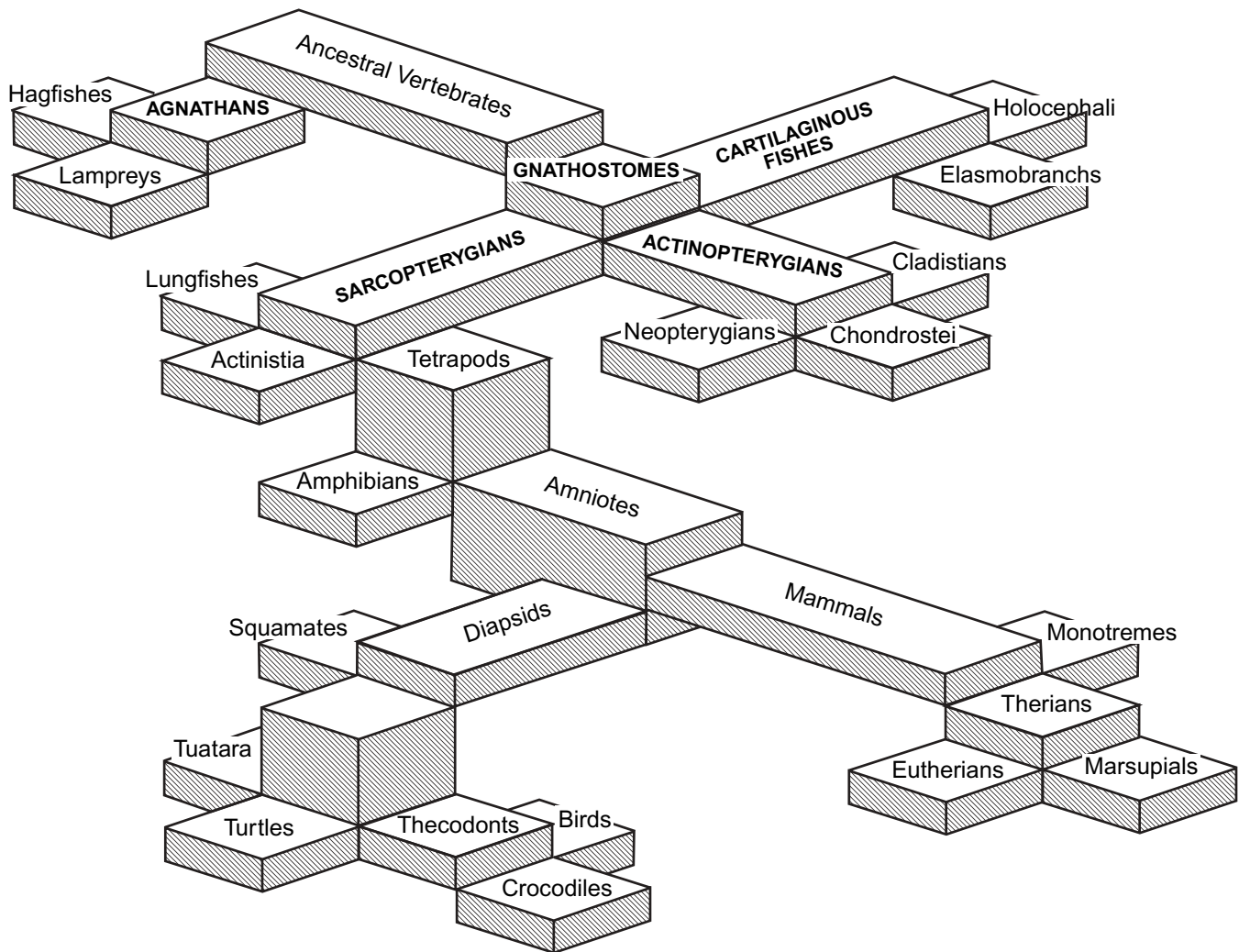


FIGURE 4-19. “Staircases” diagram of the descent of the various groups of vertebrates to emphasize that they have descended from a common ancestral stock, which is not always appreciated in the normal format of cladograms. Ancestral vertebrates are shown at the top, with the agnathan and gnathostome radiations descending from them. Within the latter are the three major radiations of cartilaginous fishes, actinopterygians (ray-finned fishes), and sarcopterygians (lobe-finned fishes and their descendants, including the tetrapods). Note that in all but one case, variation in the length and thickness of the “slabs” is merely an artistic device to keep the groups separated visually. The exception is for the amniote radiation, in which the synapsid mammals are shown diverging from the ancestral anapsid stock before the appearance of diapsids in the fossil record.

will interpret (1) whether given features are evolutionarily primitive (**plesiomorphic**) or evolutionarily derived (**apomorphic**) and (2) whether a feature present in more than one taxon is historically homologous (derived from the same feature present in a common ancestor) or homoplastic (derived independently, not having been present in a common ancestor).

Laminar Brains (Group I)

Table 4-1 lists those groups, as discussed below in the text, within each major group that have laminar brain organization. In lampreys, the vast majority of neuronal cell bodies are located within the periventricular zone throughout the brain.

Parasitic lifestyles, such as what lampreys have, are frequently associated with reduction of structures. Thus, whether the laminar organization of the brain in lampreys reflects the ancestral condition of vertebrate brains or, instead, a secondary process of reduction has yet to be established. The weight of evidence supports the theory that the earliest vertebrates were jawless, but the diversity of the now-extinct, early jawless fishes precludes assuming that their brains all closely resembled that of modern lampreys.

Cartilaginous fishes with laminar brains include cow sharks, sand sharks, spiny dogfishes, saw sharks, and angel sharks (or monkfish). They also include the chimaeras, or ratfishes. In these Group I, cartilaginous fishes, only a limited

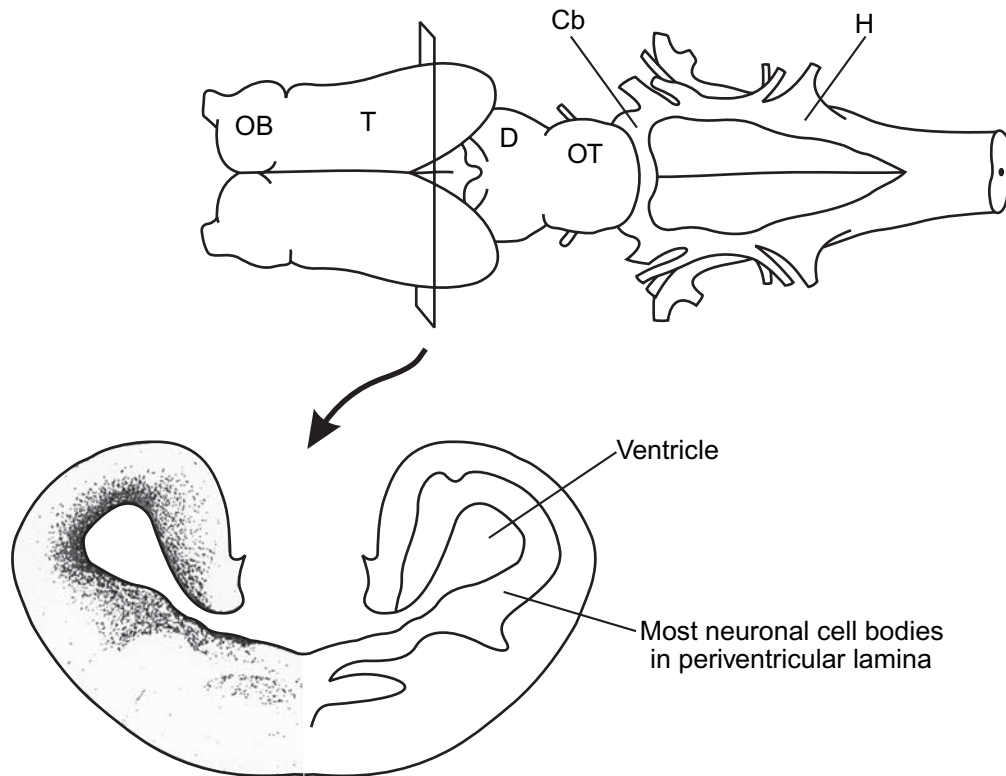


FIGURE 4-20. Dorsal view (top) of the brain of a tiger salamander (*Ambystoma tigrinum*), with the position of a transverse section through the telencephalon, shown below, indicated by the rectangle. In the transverse section, the distribution of Nissl-stained neuron cell bodies is shown on the left, and a mirror image drawing is shown on the right. Adapted from Northcutt and Kicliter (1980). Used with kind permission of Springer Science and Business Media.

migration of cells away from the periventricular surface occurs. Ratfishes are not vigorous swimmers. They live at varying depths and eat small invertebrates and fishes. Spiny dogfishes, in contrast, are voracious predators of a variety of other, fast moving fishes, such as cods and herrings. Thus, relatively simple and laminar brain organization does not necessarily preclude an active, predacious lifestyle.

Among ray-finned fishes, the brains of cladistians, sturgeons, gars, and the bowfin show only limited migration of cells away from the ventricular surface. Cladistians, sturgeons, gars, and bowfins all inhabit relatively shallow and, for the most part, fresh water, but their behavioral repertoires vary considerably. For example, cladistians are nocturnal and secretive, feeding on a variety of prey such as worms, crustaceans, and even small fishes. Gars and bowfins, in contrast, are more aggressive predators, known to move very fast in order to attack and capture other fishes for prey. It should be noted, however, that the degree of migration of neurons and the relative degree of elaboration of the telencephalon in particular represent a continuum across taxa. Gars, for example, could arguably be placed in the elaborated brain, Group II category as justifiably as in the Group I category.

Among sarcopterygii, the brains of the crossopterygian *Latimeria*, of lungfishes, and of urodele amphibians (Fig. 4-20) all show a pronounced degree of laminar organization. As in

the case of lampreys, this morphology may be the result of a secondary process of reduction, in this case related to **neoteny**—the retention of embryonic characteristics in the adult. In anurans amphibians (frogs and toads), there is limited migration of neuronal cell bodies away from the periventricular matrix.

Elaborated Brains (Group II)

Table 4-2 lists those groups, discussed below in the text, within each major radiation that have an elaborated brain organization. The brain of hagfishes is strikingly complex, in contrast to that of lampreys, with pronounced migration of cells and the presence of many large and distinct nuclear groups. Consistent with their scavenging lifestyle, hagfishes do not have complex behavioral repertoires, and the visual system is markedly reduced. They seem to use vision only for avoiding light, preferring to seek prey in the darkness. The functions and adaptive significance of their complex and enlarged brains are thus a puzzle, although complex analysis of olfactory information by the telencephalon may be a major factor (see Chapter 29). As discussed above, molecular analysis (see Box 4-1) indicates that hagfishes and lampreys are more closely related to each other than either is to jawed vertebrates and that a

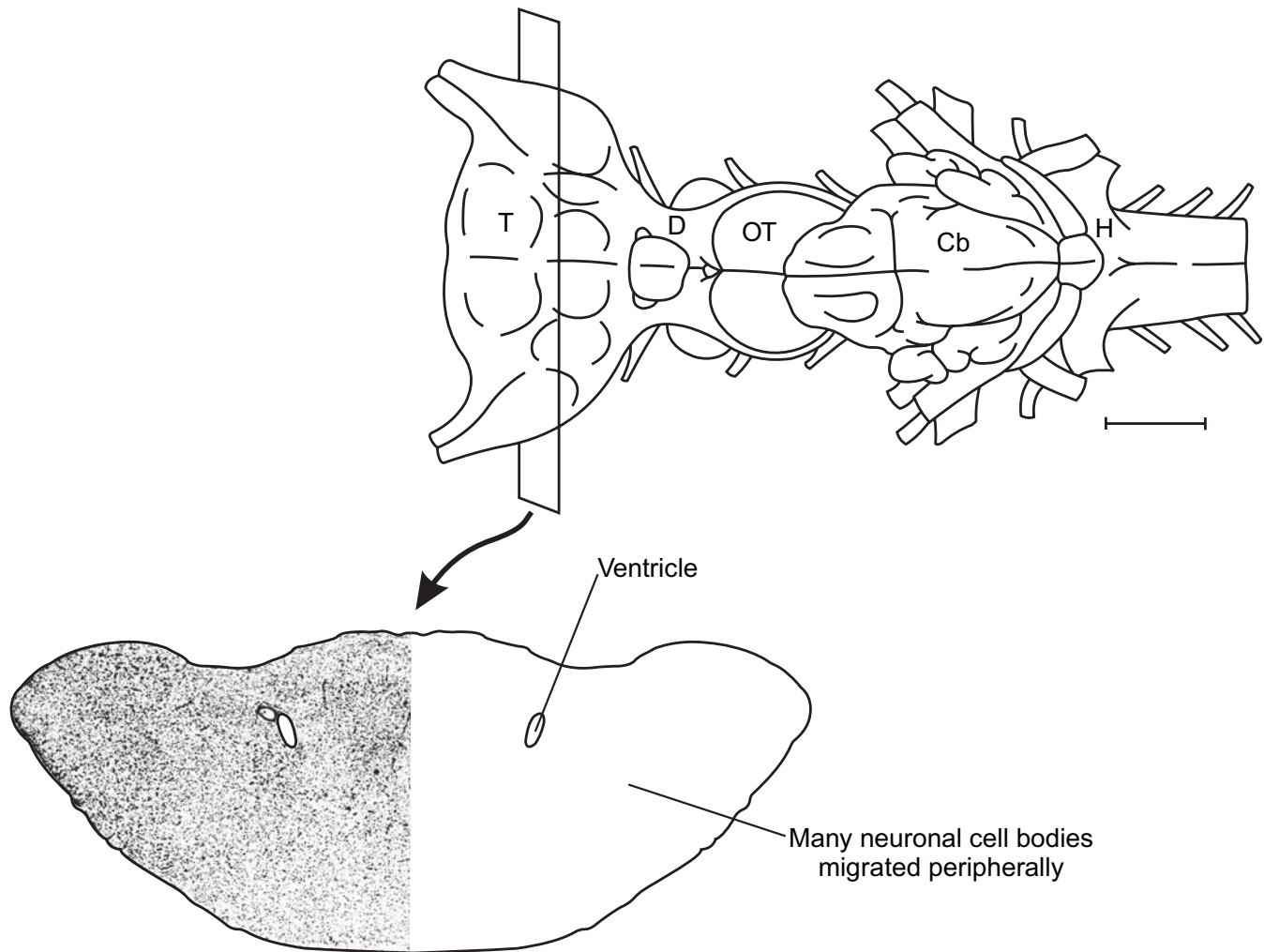


FIGURE 4-21. Dorsal view (top) of the brain of a clearnose skate (*Raja eglanteria*), with the position of a transverse section through the telencephalon, shown below, indicated by the rectangle. In the transverse section, the distribution of Nissl-stained neuron cell bodies is shown on the left, and a mirror image drawing is shown on the right. Adapted from Northcutt (1979) and used with permission of the University of Chicago Press. Scale = 5 mm.

TABLE 4-1. Vertebrates With Laminar Brains (Group I)

Cyclostomes (Agnatha)	Lampreys
Chondrichthyes	Squalomorph sharks
	Squantinomorph sharks
	Holocephalians (chimaeras)
Actinopterygii	Cladistians (reedfishes: bichirs or ropfishes)
	Chondrosteans (sturgeons and paddlefishes)
	Ginglymodians (gars)
	Halecomorphans (bowfin)
Sarcopterygii	Actinistians (coelacanth)
	Dipnoans (lungfish)
	Amphibians

TABLE 4-2. Vertebrates With Elaborated Brains (Group II)

Cyclostomes (Agnatha)	Hagfishes
Chondrichthyes	Galeomorph sharks
	Skates
	Rays
Actinopterygii	Teleosts
Sarcopterygii	Mammals
	Reptiles
	Birds

number of characters of hagfishes, such as lack of true vertebrate, are the result of secondary reduction. In contrast, the brain in hagfishes appears to have become independently elaborated to a marked degree. The range of variation in brain organization between modern hagfishes and lampreys suggests

that a pronounced variation among the ancestral jawless vertebrates also existed.

Among cartilaginous fishes, an extensive migration of neuronal cell bodies away from the periventricular surface occurs in the brains of cat sharks, requiem sharks, and hammerheads, which we refer to as galeomorph sharks. Extensive migration and complex morphology also characterize the brains of skates (Fig. 4-21) and rays. Galeomorph sharks are active predators, as are spiny dogfishes, but they also have modified jaws for deep biting and for successfully attacking larger sized prey. Skates and rays have a more sedate lifestyle, foraging for bottom-dwelling invertebrates, but also have more complex modes of locomotion. They use undulating movements of the pectoral fins (skates and stingrays) or a flapping motion of the fins similar to the motion of a bird's wing (manta rays and eagle rays). As we will see below, the nuclei involved in the coordination of motor activities are all relatively enlarged and prominent in galeomorph sharks, skates, and rays. Likewise, forebrain areas involved in sensory processing and for additional, complex behaviors, such as social interactions, courtship, and mating, are all enlarged.

In teleosts, cells are more extensively migrated away from the ventricular surface than in other ray-finned fishes. Teleosts comprise a huge and diverse radiation, and there is considerable variation in various parts of the brain among the different groups, which would fill another book or two. As we will discuss further below, teleosts include fishes that have very complex behavioral repertoires.

In amniotes, brain organization is also elaborated and complex. Among mammals, a large range of variation in brain structure and elaboration can be found, but, as in cartilaginous fishes with elaborated brains, teleosts, and other amniotes, the largest and most complex brains are in those mammals with the most complex behavioral repertoires. Among reptiles, crocodiles have the most complex behavioral repertoires known and also have the largest and most complex brains. Birds have even larger and more elaborated brains. The areas of the forebrain related to sensory processing and integration are largest in those birds with complex behavioral repertoires and/or in which learning is of particular importance, such as songbirds, crows, and parrots.

Glia and Brain Elaboration

Glial cell evolution is consistent with the independently evolved diversity of laminar to elaborated brain structure seen within each major vertebrate taxon. Mihaly Kálmán and his co-workers have studied the distribution of a particular protein, **glial fibrillary acidic protein**, or **GFAP**, in brains with different degrees of elaboration. This protein is a cytoskeletal protein of astroglia, the type of glia that either exhibits a star-shaped distribution of its processes, for which shape it is named, or maintains a slender, radial profile. These glia are involved in a variety of functions, including the induction and maintenance of the blood-brain barrier. Astrocytes may be present in areas of the brain without expressing the GFAP; nonetheless, the distribution of astrocytes that do express it varies across phylogeny.

Within each of the major vertebrate radiations—agnathans, cartilaginous fishes, actinopterygians, and the sar-

copterygian-amniote radiation—GFAP distribution varies as a function of the degree of laminar versus elaborated neural development. In brains with the more laminar type of structure, GFAP is richly distributed across most or all brain areas. In contrast, in elaborated brains, the distribution of this protein is more limited, being absent from some of the more elaborated areas, including areas within the telencephalon and dien-cephalon, optic tectum, and various parts of the hindbrain.

Laminar and Elaborated Brains Across Evolution

As the preceding discussion shows, marked variation is found in brain structure and in behavioral repertoires within each of the four radiations of vertebrates. Changes in the environment and the availability of new niches resulted in the current range of variation by providing new evolutionary opportunities. The opportunistic nature of evolutionary change results in a great deal of variation both within and among the various taxa, rather than “trends.” The approach that we have taken here, in first considering all Group I taxa with laminar brains and subsequently considering all Group II taxa with elaborated brains, will avoid the trap of *scala naturae* thinking and the fantasy of a single, directed, linear progression toward an anthropocentrically defined “goal,” namely, human beings. Variation present *within* each group is as important and meaningful as the variation *between* groups. The old idea of a fish-to-frog-to-rat-to-cat-to-monkey-to-human “progression” is neither historically accurate nor evolutionarily meaningful. Such notions should be filed on the reader's shelf in the appropriate place—next to Bullfinch's Mythology.

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5

Evolution and Adaptation of the Brain, Behavior, and Intelligence

PHYLOGENY AND ADAPTATION

When we think about evolution, we usually have phylogeny in mind; that is, how different lineages are related to each other, how they have changed through time, and what their similarities and differences are. We typically do not consider the mechanisms by which such similarities and differences have come about except in the general sense of adjustment to environmental change. The general process by which a species adjusts to environmental change is known as **adaptation**. Adaptation to changing environmental conditions, however, is not the only situation that results in evolutionary change; sometimes a random change in a population, such as a shift in the direction of longer legs or more acute vision enables a species to begin to take advantage of environmental opportunities that were present all the time. Such “lucky accidents” then can serve as a stimulus to enhance the trend started by this chance occurrence to take still further advantage of the existing environment.

The usual approach to studying evolution of the nervous system, behavior, or any other characteristic that has a genetic basis is to perform a comparative study. Although studies of fossils can be useful for some purposes, research on neural or behavioral evolution usually involves extant animals. Comparative studies involve research on a number of species that have something in common. When the basis for choosing a species for study is their lineage or degree of relatedness, the comparative study is being done in a phyletic context, and the investigators hope to learn something about the historical development of that lineage by studying its living representatives. This, however, is not the only reason to do comparative

studies. One also could choose animals irrespective of their descent from a common lineage, because they vary in the degree to which they have some specific characteristic. For example, the animals could be chosen because they vary in the extent of development of their color vision or hearing, or they might be chosen because they vary in the size of some brain structure. Such structure-function studies are vital for understanding how phyletic changes might have occurred. An important consideration in adaptation studies is that, unlike phyletic studies, the researchers need not necessarily concern themselves with the phyletic relatedness of the subjects. Indeed, similar environmental pressures have resulted in the independent development of remarkably similar adaptations in quite unrelated species. Thus, phyletic comparative studies are concerned with *what* has changed in a specific lineage; adaptation comparative studies are concerned with *how* such changes might have come about. Both types of comparative investigation are important for understanding the complete picture of evolutionary change and development.

Phyletic Studies

Phyletic comparative studies are those that attempt to reconstruct the evolutionary history of the development of some portion of the nervous system or perhaps of a particular behavior pattern in a given lineage. To do such studies, we must select animals that represent specific lines of descent in the evolution of a particular lineage. The most successful studies of this type are often limited to a fairly restricted lineage such as different species within a family or families within an order. In addition, the successful studies tend to compare large numbers of species. Those that study animals that are less

closely related, such as those making comparisons at the class level (fishes vs. mammals vs. birds, etc.), often tend to be less successful because of the difficulty of finding two or three species that are truly representative of such a broad aggregation of characteristics as would be found in a class.

Why are historical reconstruction studies important? First, because of the human fascination with where we have come from—the same passion that guides all historical research. Can we say, for example, that a particular neural structure or process or even behavior pattern is uniquely characteristic of mammals or is solely possessed by carnivores or primates? Are there systematic differences between closely related families of rodents or birds? Are there general trends or levels of organization that are characteristic of certain lineages, such as the ray-finned fishes?

A second reason for understanding these historical trends is that they can yield important clues to the relationship between the specific behavior patterns that are used by an animal and the structure and organization of the central nervous systems that make this behavior possible. Thus, comparisons of the anatomy and physiology of related animals that vary in the extent to which they perform certain behaviors is a powerful research strategy that often can provide important clues to how the system works. In particular, much can be learned from the comparison of species that are highly specialized for a specific function with those that are less well adapted. Figure 5-1 illustrates how this approach can be used. This figure is based on the work of Leonard Radinsky, who studied the cerebral cortex of a number of species of otters. He ranked the species according to the extent to which they used their forepaws to manipulate food objects. He then observed how this ranking matched up with the somatosensory (e.g., touch and temperature) area of cortex devoted to the representation of the forepaws. Figure 5-1 presents representatives of the extreme ends of the rank order. The brain labeled A is from an otter species that makes extensive use of the forepaws in manipulation of food; the brain labeled B is from an otter that makes relatively little use of the forepaws for food manipulation. Each diagram also shows the sensory representation of the face. The amount of area devoted to the face is roughly the same in the two species, but a major difference can be seen in the amount of somatosensory cortex devoted to the forepaw. The animal shown in A has a much larger forepaw representation than does the animal shown in B. This relationship between the extent to which a body part is used and the amount of brain tissue associated with it will be discussed again later in this chapter.

Adaptation Studies

Although the two species shown in Figure 5-1 are closely related, commonality of lineage is not necessarily an important consideration in adaptation research strategy. Because species often solve similar survival problems in similar ways whether they are related or not, all that matters in this approach is that each has evolved a particular level of development of the structure or process under investigation. An illustration of the independent evolution of similar neural and behavioral processes may be seen in the comparative anatomy and comparative behavior of electroreception. This sensory system has inde-

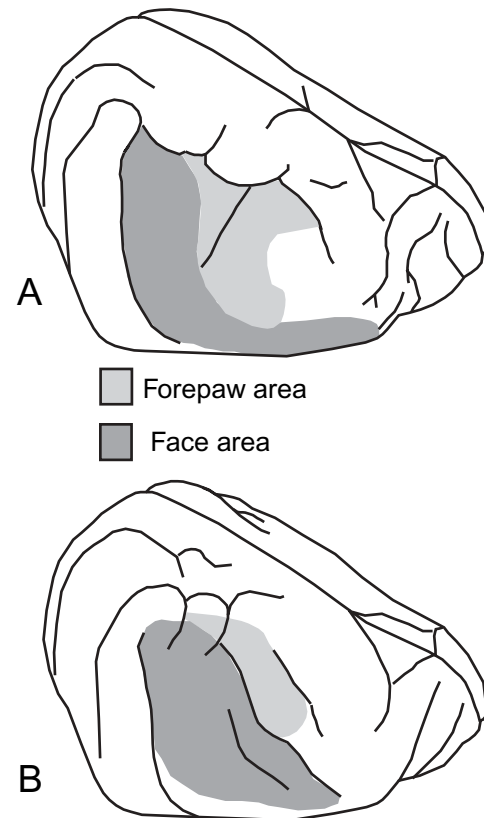


FIGURE 5-1. The representations of the face and hand area in the somatosensory cortex of two species of otter. Species A uses its forepaws more extensively to manipulate food objects than species B. Although the representations of the face are about the same in both, the area of cortex devoted to the forepaws is greater in A than in B. After Radinsky, 1968 and used with permission of John Wiley & Sons.

pendently evolved a number of times among remotely related groups of fishes as well as in other vertebrate classes, including mammals. Likewise, infrared detection has evolved independently in relatively unrelated groups of snakes. One could, for example, study species that vary in their relative degree of sensitivity or other characteristics of electroreception or infrared reception in relation to the relative size or degree of development or organizational elaboration of the neural structures that underlie these senses as an adaptation study. This study need not make any reference to the historical lineages of the individual species studied and would provide useful information about structure-function relationships. An error that is too often made, however, is to assume when behaviors or structures are examined in rank order that this sequence necessarily represents the historical sequence in which the system evolved.

An important benefit from adaptation studies is that the particular way certain species have adapted or *failed to adapt* to the pressures of their environments makes them very useful as models for normal developmental processes as well as models for various pathological states, usually in humans. For example, about 20% of White Carneau pigeons have difficulty in discriminating between patterns that are mirror images of

one another, such as ⟨vs.⟩ or [vs.], yet they have no difficulty discriminating patterns that are not mirror symmetrical, such as + vs. =. The failure of these birds to easily tell mirror-symmetrical patterns apart makes them useful as a model for the human reading disorder known as dyslexia, in which readers have difficulty telling apart the letters **p** from **q** and **b** from **d**. Such animal models can offer important clues to the morphological basis of this disorder and can provide a useful model system on which to test therapies.

Finally, another benefit of adaptation studies is that they frequently reveal unique experimental situations that permit experimenters to perform experiments that they otherwise could not. Three well-known examples are:

- The squid giant axon, which allowed neurophysiologists to investigate the properties of the axonal membrane directly by providing a preparation with an axon diameter big enough to allow insertion of an electrode.
- Individually identifiable neurons, which allow experimenters to investigate the same neuron in animal after animal.
- Vocal-learning pathways in the brains of birds, which have permitted the elucidation of the complex central pathways from the auditory receptors in the medulla to the vocalization control regions of the telencephalon and back to the motor neurons of the medulla that control the actual production of sound.

The Phylogenetic Scale

As discussed in Chapter 1, a notion that has misguided comparative studies has been the concept of the **phylogenetic scale** or evolutionary scale, which is derived from the medieval idea of the *scala naturae* (scale of nature) with a deity at the top, angels next, humans somewhat lower, and then apes, monkeys, and assorted other animals that differ progressively in their resemblance to humans as the scale is descended. After the success of the Darwinian revolution, and the acceptance of the idea of evolutionary change in the scientific community, this notion served as the model for evolutionary change for many who had little knowledge about the history of animal evolution. One can readily see how this could come about: land animals came from the sea, reptiles gave rise to mammals (as was then believed), apes gave rise to humans, and so on. While these ideas are correct in a vague sense, they foster serious misunderstandings about the history of vertebrate evolution and they lead to very poor choices of species to study in a phyletic context. The scientific literature is filled with erroneous conclusions, sometimes by distinguished scientists, about evolutionary changes based on comparisons of a goldfish, a frog, a lizard, a rat, a cat, a monkey, and a human—a sequence that bears little resemblance to an actual genealogical lineage as understood by modern paleontologists.

Figure 5-2 shows the type of hierarchical arrangement that derives from *scala naturae* thinking. Each species occupies a niche on this hierarchical staircase in which a higher position denotes both more recent evolution and greater evolutionary advancement or development. The inherent fallacy of this model is that it assumes that more ancient life forms are more

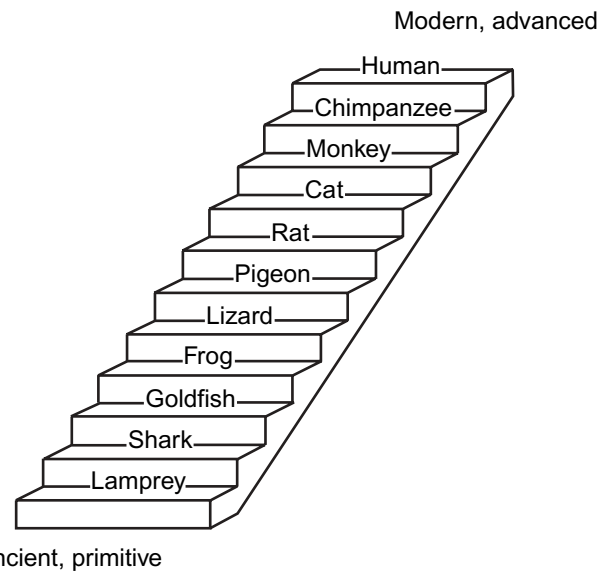


FIGURE 5-2. A phylogenetic scale of vertebrates. Those animals at the bottom of the scale are regarded as phylogenetically older and more primitive. Those at the top are regarded as being more modern and more advanced.

primitive than more recent forms. Although there can be no doubt that evolution has resulted in some dramatic improvements in the design of brains and bodies, one should not necessarily assume that ancient, ancestral forms were “primitive” in the sense of being crude and poorly adapted versions of modern animals. Animals generally were well adapted to their environments at whatever geological age they may have existed, and many of the adaptations of ancestral forms were quite sophisticated and efficient for the environments in which they lived. Indeed, we should only speak of “primitive” characteristics, not “primitive” species.

The Phylogenetic Tree

Figure 5-3 shows the way a systematic biologist would view the relationships among the animals shown in Figure 5-2 and many of their vertebrate relatives. Not all vertebrate taxa are shown in this tree. For a more complete phylogeny of the vertebrates, see Chapter 4. The figure is a family tree of animal species that shows how closely or remotely various animal groups are related and what the basis of the relationship is. In this model of evolution, the location of a group of animals on the tree only indicates the group’s relative time of appearance in the fossil record; that is, the age of the oldest fossilized remains of the lineage thus far discovered. The vertical extent of the figure represents time with the present era represented at the top and more ancient eras represented below. The vertically oriented lines indicate lineages or branches on the family tree. Each of the animals indicated in Figure 5-2 is shown on its appropriate branch of the family tree. The complexity of the animals is not indicated in any way in this figure, nor are such judgmental evaluations as “advancement” or “progress” represented.

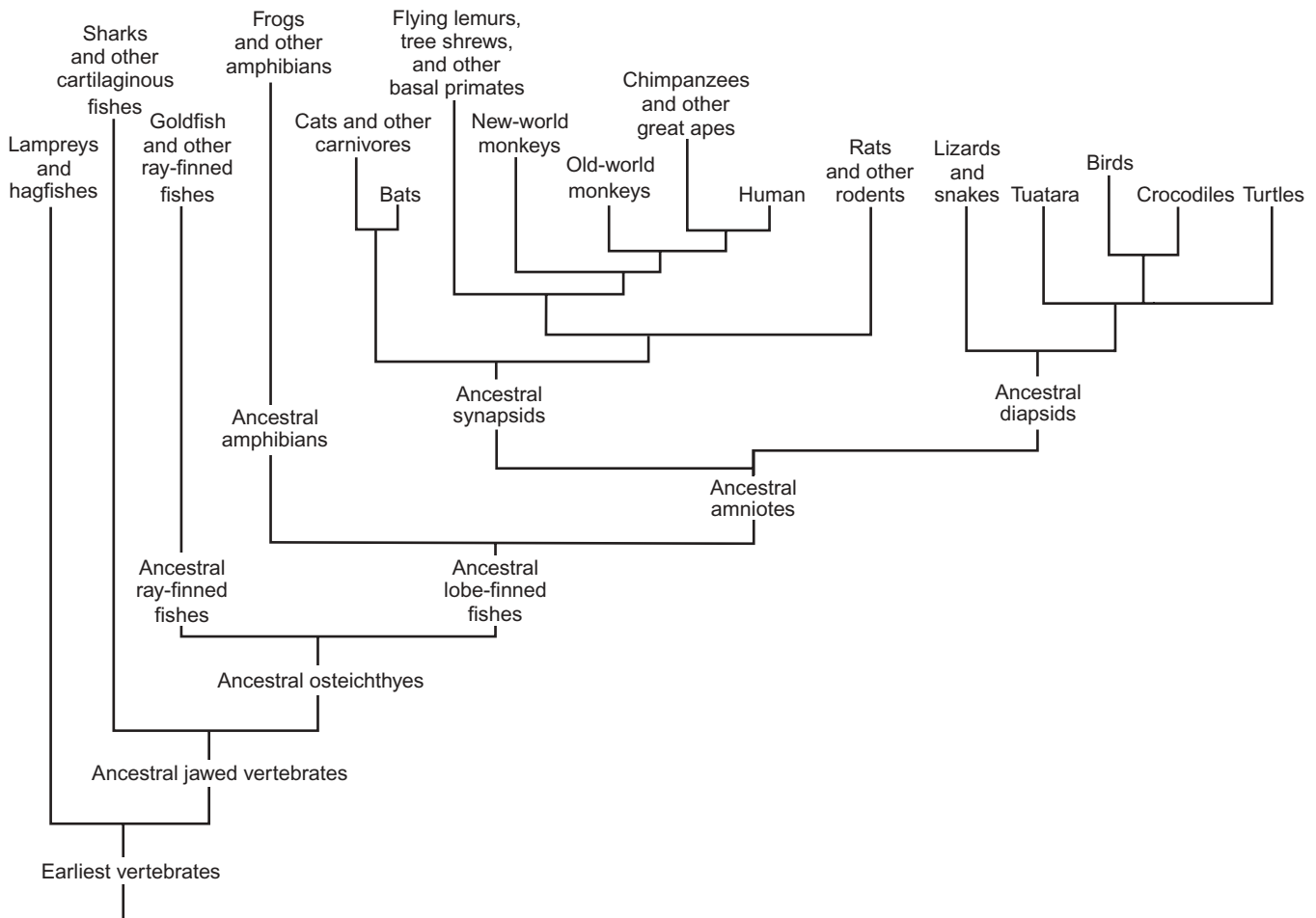


FIGURE 5-3. A phylogenetic tree of selected groups of vertebrates. The ancestral animal groups represented at the bottom of the tree are phylogenetically older than the full set of those in the top third of the tree. Evolutionary advancement or progress is not indicated on this diagram.

One can see in this figure the four great lineages of the vertebrates represented as vertical lines in the left half of the figure: the jawless fishes leading to modern lampreys and hagfishes, the cartilaginous fishes leading to modern sharks and rays, the ray-finned fishes leading to modern ray-finned fishes, and the lobe-finned (fleshy-finned) fishes leading to the modern amphibians and amniotes. Because these four lineages evolved independently from one another (i.e., they developed in parallel), members of one group should not be used to represent a stage of evolution in another group. Thus, no modern ray-finned fish should be used to represent a stage in the development of any tetrapod (amphibians, mammals, reptiles, and birds). The same would apply to the modern sharks, which are members of the cartilaginous fish lineage. While these animals are descendants of very ancient lineages and can give some clues to what the earliest vertebrates were like, they are not members of the lineage that eventually produced land vertebrates.

Similar considerations apply within the land vertebrates. One should not study an extant reptile, such as a lizard or turtle, in order to gain understanding of what the ancestors of

mammals were like. As discussed in Chapter 4, the amniote line leading to modern reptiles evolved *after* mammals, so extant lizards or turtles could hardly represent mammalian ancestors.

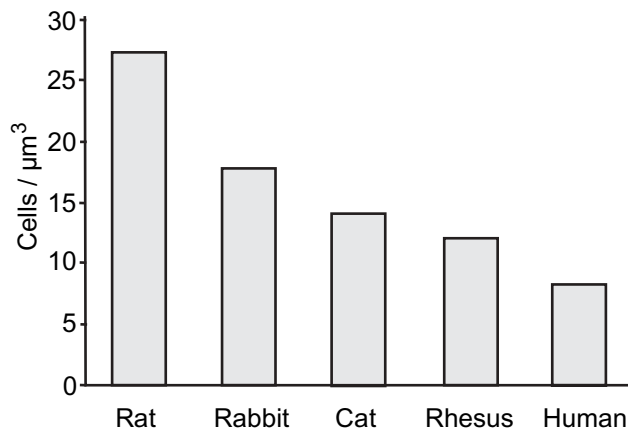
Table 5-1 compares the differences between the phylogenetic tree and the phylogenetic scale as models of animal evolution and development. The two approaches to the systematic arrangement of living animals give very different sorts of information. The phylogenetic scale gives information that tends to be evaluative, whereas the phylogenetic tree gives information that is historical. Because the scale is a ranking, it is unilinear or unidimensional, whereas the tree model emphasizes the multilinearity of evolution and the radiation of lines of descent from common ancestral points.

COMPLEXITY AND EVOLUTION

One of the features of vertebrate evolution that has led to misconceptions is the observation that mammals in general and primates in particular seem to be the most complex, but this is probably only because they have been the most intensively

TABLE 5-1. A Comparison of the Phylogenetic Tree and the Phylogenetic Scale as Models of Evolutionary Change and Development

Phylogenetic Tree	Phylogenetic scale
Multilinear	Unilinear
Based on scientific judgments	Based on scientific and value judgments
Nonhierarchical (animals not ranked)	Hierarchical (based on a ranking)
Presumed historical sequence is determined by historical data (the fossil record)	Presumed historical sequence based on increases in complexity
Complexity is independent of time; increased complexity and increased simplification can both be evolutionary trends	Complexity increases with time

**FIGURE 5-4.** The relative number of Purkinje cells in the cerebellar cortex in five species of mammals. Data from Lange (1975).

studied. When detailed studies are made of nonprimate mammals or of nonmammals, levels of complexity as great, or sometimes greater, than those of mammals emerge. For example, olfaction in many nonprimate mammals and audition in echo-locating bats and marine mammals are far superior to those senses in primates. Birds are superior to most mammals in many aspects of their vision. The cerebellum is a far more complex organ in mormyrid fishes than it is in any mammal. The speed and accuracy of the frog tongue as an organ for prey capture surpasses any response capability of primate somatic motor responses.

Another often misunderstood point is that although evolution frequently has produced an increase in complexity of brain organization and behavior, the earliest vertebrates were already quite complex animals in comparison to their invertebrate ancestors and were quite well adapted to their environments. Likewise, some invertebrates have very complex brains in their own right. Often, by choosing too limited a range of species, investigators give a false impression of a trend from simple to complex. An example of how too narrow a selection can produce a false trend in the data can be seen in Figure 5-4. This figure shows the number of Purkinje cells (large neurons located in the cerebellum) per cubic micrometer of cerebellar cortex in five species of mammals based on a study by Winfried Lange. These particular mammals were selected for the figure

from among 20 species of mammals reported by Lange because they represent a typical phylogenetic-scale sequence. If one were to assume that this sequence actually represented evolutionary history, which indeed it does not, the sequence would suggest that there is a trend in the evolution toward humans of a decreased number of Purkinje cells in the cerebellum. Moreover, because many humans believe themselves to represent the pinnacle of evolutionary advancement, a logical conclusion would be that there must be something inherently better in having fewer Purkinje cells.

If one now looks at Figure 5-5, we see the same data represented, but with some additional species from Lange's report included. We see that the squirrel monkey, which is a primate, has about the same relative number of Purkinje cells as does a cat or a fox, which are carnivores and supposedly lower animal forms. Moreover, a domestic bull has the same relative Purkinje cell number as does the supposedly higher rhesus monkey. Finally, the number of human Purkinje cells is nicely matched by the relative number of such cells in an elephant. How can we interpret this? Lange's report tells us that there is an inverse relationship between relative Purkinje cell number and the absolute size of the cerebellum. Indeed, 80% of the variability in Purkinje cell number is due to the variability in cerebellum size. So rather than indicating a trend in the direction of human perfection, Lange's data mean that Purkinje cell number is dictated by cerebellum size. Similar data exist in birds, in which the cell counts in the ostrich cerebellum are comparable to those of the pilot whale, and those of the titmouse (a very small bird) exceed even the values for rats and mice.

Anagenesis

Another influential idea in comparative research is the concept of **anagenesis**, which was introduced into the biological literature in the late 1950s and refers to progressive advancement or improvement through time in a given lineage. Anagenesis is derived from notions, prevalent since the fifteenth century at least, that the European body type, as well as European social systems, religion, and culture, represent the pinnacles of human development. All others are supposedly inferior and less perfectly formed. These highly anthropocentric, homocentric, and Eurocentric views have, on more than one occasion, lead to data being interpreted to suggest that humans are at the top of the hierarchy. Here is a quotation from

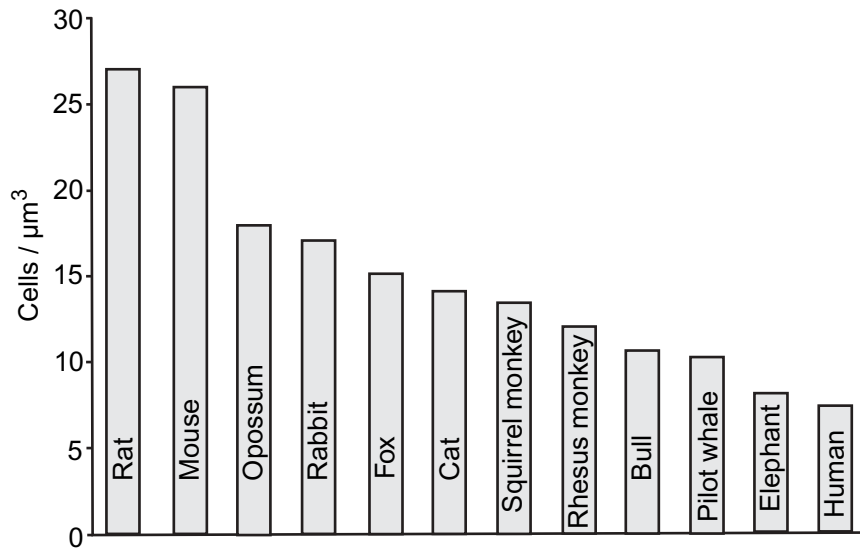


FIGURE 5-5. Seven additional species of mammals have been added to the data shown in Figure 5-4. Data from Lange (1975).

Lange, the comparative neuroanatomist whose cerebellum data were shown in Figures 5-4 and 5-5. He offered the following lament in the discussion of an inconvenient result: "If the number of cells per unit volume alone is taken into account as the only parameter for the organization level of a brain, the elephant or some aquatic mammals would appear to show a higher degree of brain evolution than man." There is, however, no biological reason for humans necessarily to have the highest degree of brain development or psychological performance. This is not to say that humans are not very unique creatures. Nevertheless, in spite of our special characteristics that have permitted us to arrive where we are today (for good or for ill), we do not have a monopoly on special or unique characteristics, nor are we always to be found at the pinnacle of every hierarchical ranking.

Figure 5-6 presents data that will help you to keep some perspective on the idea of human perfection. The figure shows the relationship between the area of the largest region of the cerebral cortex, known as the **neocortex**, and the volume of the brain as a whole in mammals. The figure shows that, as brain volume increases, the area of the neocortex increases proportionately. What about the neocortex of humans? Our large neocortical mass is often pointed to as a sign of our superior intellectual abilities compared with other mammals. The figure, however, indicates that human neocortex falls close to the regression line for mammals. In other words, we have no more neocortex than would be expected for a mammal with a brain of our size. To be sure, humans do have greater amounts of certain regions of the neocortex than would be expected from their brain size, and certain structures in the depths of the brain are also greater in size than would be expected from such curves, but in terms of total area of the neocortex, we are not in any way special for our size.

Another problem with the anagenetic approach is that it is highly dependent on value judgments on the part of the observer as to what constitutes progress or advancement.

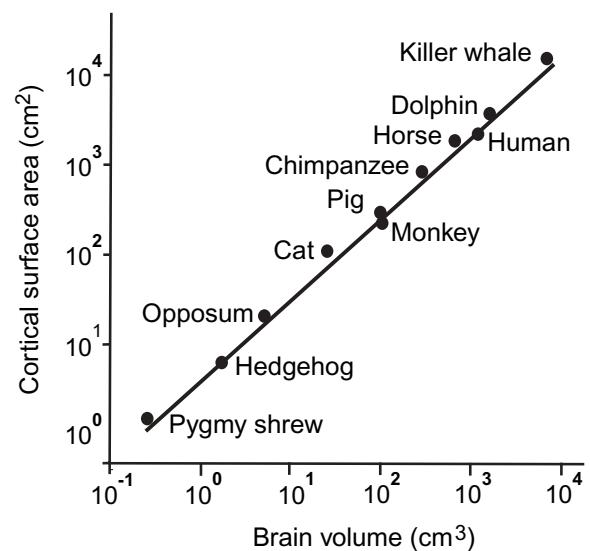


FIGURE 5-6. A regression line of the cortical surface area and brain volumes of 50 species of mammals, of which only 11 representative species have been indicated. Although larger brains have more neocortex than do smaller brains, humans have the total cortical area that would be expected from their brain size. Adapted from Jerison (2001a) and used with permission of Cambridge University Press.

The study of evolution has taught us, however, that the same adaptation to the environment in one circumstance can be the road to the development of a new species but in another circumstance leads inexorably towards extinction. There is nothing progressive about an adaptation in itself; it is the circumstances (i.e., the selective pressures) that make adaptation progressive. Anything that helps an animal to survive is "progress," whether it is based on increased complexity or increased simplification.

Grades of Evolutionary Advancement

The unit of anagenetic analysis is the “grade,” which has been variously defined but is generally conceded to be a progressive improvement in a characteristic through a specified lineage. Figure 5-7 presents some comparisons from published data on various species of bats. The figure shows the relative size of the olfactory bulb (the volume of the olfactory bulb as a proportion of the volume of the cerebral hemisphere) in 40 different species of bats arranged according to their diet. The relative olfactory bulb sizes have been sorted according to whether the bats are insect eating, flesh eating, fruit eating, or fruit and insect eating. Since the majority of bats are insectivorous, these have the highest representation. The two groups of bats that are not fruit eaters have significantly smaller olfactory bulbs than do the two groups that have fruit as the exclusive or major part of their diet. One thus could consider that bat olfactory bulbs have two grades: an insect-flesh eating grade and a higher fruit eating grade, which is characterized by larger olfactory bulbs.

Unfortunately, the notion of evolutionary “progress” suggests an advancement from simple to complex, which in turn leads to a tendency to conclude that the more “advanced” level was the more recently evolved. Evolutionary history, however, is filled with nonlinearities in which a seemingly less complex form evolved from one that seemed more complex. One example is the evolution of the heart. Fishes have a two-chambered heart, amphibians and most reptiles have a three-chambered heart, and birds and mammals have a four-chambered heart. This progression would seem to suggest three grades of heart based on the number of chambers:

- Fish grade, which consists of a two-chambered heart.
- Amphibian-reptile grade, which consists of a three-chambered heart.

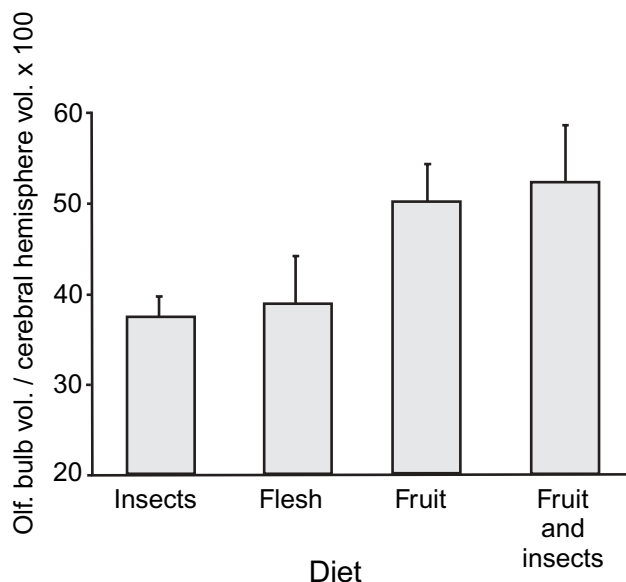


FIGURE 5-7. Relative size of the olfactory bulb in bats arranged according to their diet. Fruit eating bats have significantly larger olfactory bulbs than do insect or flesh eating bats. Data from Bhatnagar and Kallen (1974).

- Avian-mammalian grade, which consists of a four-chambered heart.

On the face of it, this would appear to be a simple ranking of progressive advancement: two chambers, three chambers, and four chambers. But in fact, four chambers evolved directly from two chambers, and three chambers is an adaptation of four chambers rather than its predecessor. Modern evidence suggests that the four-chambered heart was already present in the immediate ancestors of land vertebrates. Thus, the earliest land vertebrates had a four-chambered heart. These four chambers, however, like most fish hearts today, were arranged in a linear sequence, quite unlike the four-chambered hearts of amniotes. The three-chambered heart of modern amphibians (who are not especially close relatives of the amphibian ancestors of mammals, reptiles, and birds) evolved, in part, as a consequence of the amphibian reliance on the skin as a supplementary respiratory organ in addition to lungs. Nevertheless, modern studies of the amphibian heart indicate that its three-chambered organization is quite efficient at keeping the oxygenated and unoxygenated blood streams separated by means of differences in their times of arrival into the heart's single ventricle. An important lesson about evolution may be learned from this example: simplification (or apparent simplification) of a system can be just as adaptive (or progressive) as increasing complexity.

A second example comes from grades of primate social behavior. Four grades have been noted:

- Solitary living.
- Harem system (one male and many females).
- Multiple males and females.
- Pair living.

Some might rank pair living as the highest grade since it is the one with which we identify most closely in Western societies. Any sequence, however, could be a plausible representation of the evolutionary history of primate social groupings and indeed all four of these grades can be found as widely distributed among the prosimians as among the simians and even among the hominoids, namely, the great apes and humans. If this were an evolutionary sequence, however, we would expect solitary living to be most widely distributed among the prosimians with the higher grades increasing in frequency in the groups most closely related to humans.

Our intention is not to leave you with the conclusion that grades have no utility in comparative research. Grades can be quite useful in analyzing structure-function relationships. We must not fall into the trap, however, of assuming that the sequence of grades necessarily represents the historical development of the characteristic under study.

EVOLUTIONARY CHANGE

How do evolutionary changes come about and how are they reflected in the central nervous system? As we discussed in Chapter 1, evolutionary change often has its roots in pressures from the environment, either internal or external,

although random mutations also can have great effects if they are not too quickly diluted in a large population. Environmental pressures can arise from decreased availability of food, increased presence of predators, increased competition for mates or nesting sites, and so on. Sometimes ample food supplies are available but only to those who have the capability to gain access to them. Environmental pressures do not directly produce somatic or central nervous system changes; the changes have to occur independently, even if only to a limited extent, so that natural selection can operate on them. Some of these conditions exist as a byproduct of some other evolutionary trend. For example, the jaw bones that evolved into ear ossicles arrived at a location in the jaw where they could come under selective pressures that favored sound conduction not because the auditory system needed them but because of selective pressures related to feeding. Once they were in an appropriate position, a major evolutionary change occurred when their role in sound conduction became more advantageous to the animals' survival than did their role in feeding.

Let us return to the example of the use of forepaws that we discussed in connection with Figure 5-1. If more dexterous forepaws give access to ample food supplies, those creatures that already have slightly more dexterous paws than their fellows have a better chance of surviving long enough to reproduce and successfully rear their young, who will carry the genes for those more dexterous forepaws. This process is shown diagrammatically in Figure 5-8. Of course, concurrent with the increased mechanical agility of these paws is the increased ability of the nervous system to control those paws with increased precision. As the figure indicates, if an advantageous tendency is already present in the gene pool, it will be selected for; if not, and if the environmental pressure is life threatening, the result will be extinction. Indeed, extinction is a very common event in evolution. If these changes in the forepaws and their corresponding central nervous system adaptations can be put to good behavioral use to more effectively

interact with the environment, the environmental pressure will be reduced and the probability of successful reproduction of successive generations will increase.

While subtle central nervous system changes could occur without being reflected in somatic changes (such as changes in dendritic or columnar organization in the cerebral cortex), the reverse (somatic changes without corresponding central nervous system changes) would be highly unlikely. To use a computer analogy, there is no point to adding more sophisticated peripheral devices to your computer if the computer lacks appropriate hardware and software to take advantage of the added sophistication of the peripheral devices.

BRAIN EVOLUTION AND BEHAVIORAL ADAPTATION

Most evolutionary biologists probably would agree that those animal species that are alive and flourishing today are uniquely adapted to the lives that they lead. Their brains are no less adapted than are other parts of their bodies. The brain is the executive organ of behavior, and often behavior plays a vital role in successful adaptation. Moreover, orderly relationships can be seen among differing levels of development, even in remotely related animals. For example, a vertebrate that uses its snout as an exploratory organ, whether it is a shark, an alligator, or a pig, will have highly developed sensory innervation of the skin on the snout and a well-developed trigeminal cranial nerve. A fish, a lizard, or a mammal with a well-developed sense of smell will have a complex and highly organized olfactory system. A vertebrate with a powerful and adroitly used tail and/or hind limbs will have a large, well-developed lumbar spinal cord.

Successful adaptation to the environment often means behavioral adaptation. Behavioral adaptation means brain adaptation. Overlaid upon a general vertebrate organization are the unique adaptations of the individual species. Animals (whether closely related or not) that have responded successfully to environmental challenges in similar behavioral ways frequently have accomplished their adaptations by having evolved remarkably similar neural substrates. Although much has been made of the rather impressive differences between the brains of different vertebrate groups, when seen in the broader context of a generally consistent overall organization with sporadic, highly specialized adaptations, the differences seem less important, and the nervous system appears to have had a relatively conservative evolution.

Brain Size and Brain Allometry

When looking at the brains of different animals, the first thing that impresses the observer is the dramatic variability in brain size both within and between different vertebrate taxa. Further examination will indicate that the largest brains tend to belong to the largest animals. In other words, the brain, like other organs of the body, tends to be scaled appropriately to the animal's body size. **Allometry** is a mathematical method for allowing comparisons of the relative size of body parts by effectively removing the influence of body size. In other words,

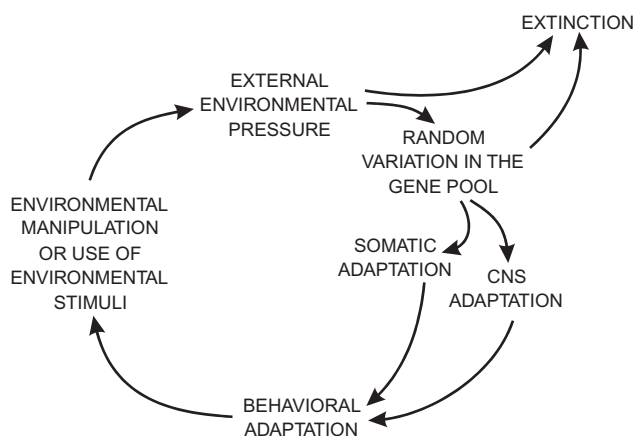


FIGURE 5-8. The cycle of environmental pressure and evolutionary change. Life threatening environmental pressures that do not act on appropriate variations already present in the gene pool of a species will lead to extinction. If the appropriate conditions are present, even to a small degree, they can be selected for to result ultimately in some reduction of the environmental pressure.

brain allometry permits us to see which animals have brains that are larger or smaller than would be expected for their body size.

Brain Allometry. Figure 5-9 shows an allometric, double logarithmic plot of relative brain size from a number of vertebrate classes. The figure shows the average weight of the brain in grams plotted as a function of the average weight of the body in grams. Within these axes are groups of convex polygons. Each polygon is the outer boundary of a set of data points that represent the individual species of the vertebrate class that is contained within it. Average-weight brains lie along a regression line (not shown in the figure) that passes through the middle of the polygon from lower left to upper right.

The figure represents data from the brains and body weights of 647 mammals, 1,027 ray-finned fishes, 41 amphibians, 59 reptiles, and 15 agnathans (jawless fishes). These data are a compilation of measurements collected by Harry Jerison, a comparative neuroscientist and specialist in brain allometry, and data provided by other neuroscientists. The results of this analysis are quite revealing. First, note that the brains of many ray-finned fishes, which usually are assigned a rather lowly position on the “phylogenetic scale” of vertebrates, have brains that are comparable in relative size to those of reptiles of equivalent

body weight. Moreover, the upper surface of the ray-finned fish polygon is moderately higher than the upper surface of the reptile polygon. This indicates that the brains of the largest bony fishes, located along the top surface of the fish polygon, are heavier than are the brains of some reptiles of equivalent body weight. In contrast, the jawless fishes have brain weights that overlap the lower end of the ray-finned fish polygon. Note that cartilaginous fishes, which are usually placed rather low on the “phylogenetic scale” and are commonly regarded (though perhaps unfairly) as rather stupid, actually have brains that are relatively large; some are comparable in size to those of mammal and bird brains from species with equivalent body weights.

Higher up in the figure is the polygon representing the mammals. The primates, which are at the top of the “phylogenetic scale,” have brains that are located in the upper half of the mammal polygon, but for the most part, this order of mammals is only modestly above the average for mammals in general. The top surface of the mammalian polygon is occupied by the animals that are often regarded as having high intelligence: humans, porpoises, elephants, and whales. However, chimpanzees and gorillas, both close relatives of humans and considered to be quite intelligent, are only average among the mammals in relative brain size.

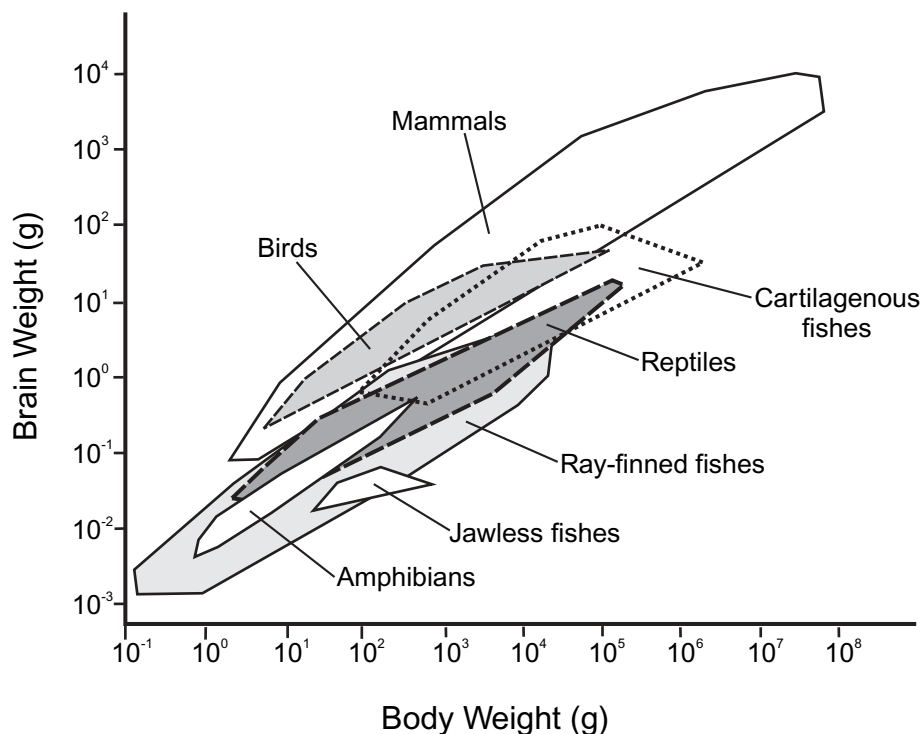


FIGURE 5-9. Log brain weight plotted as a function of body weight for 2,018 species of vertebrates. The geometrical figures are the minimum convex polygons that enclose all of the data points. Data are shown for jawless, cartilaginous, and ray-finned fishes, reptiles, birds, and mammals. Data points that lie along the long axis of each polygon represent species that have a brain weight that would be expected from their body weight. Those at the top of the polygon have brain weights that are greater than would be expected from their body weights. Conversely, those at the bottom of the polygon have lower than expected brain weights. Adapted from Jerison (2001a) and used with permission of Cambridge University Press.

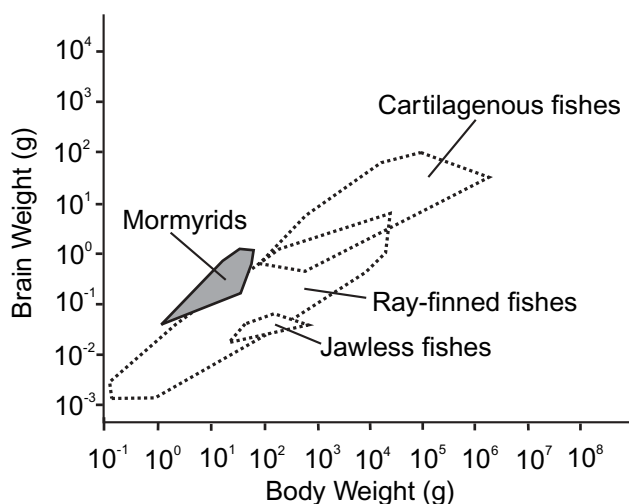


FIGURE 5-10. An allometric plot of brain weight-body weight data for 11 species of mormyrid fishes, which are electroreceptive and have exceptionally large cerebella. The minimum convex polygons for jawless, cartilaginous, and ray-finned fishes from Fig. 5-9 have been drawn with dotted lines for reference. Adapted from Jerison (2001a) and used with permission of Cambridge University Press.

The bird polygon shows an impressive amount of overlap with the mammalian polygon, especially among the smallest birds and mammals. In this region, the polygons indicate that small birds and small mammals of comparable body weights have the same weight brains. Not only that, but the birds with the largest brains, such as parrots, have brains that would be regarded as typical of a small primate of the same body weight. However, as is the case with chimpanzees and gorillas, pigeons, which exhibit many, complex cognitive behaviors (as further discussed in Box 25-3), are only average among birds in relative brain size.

Figure 5-10 includes the same polygons representing the brains of cartilaginous fishes, ray-finned fishes, and jawless fishes as were shown in Figure 5-9. In addition, a polygon representing mormyrid fishes has been included. These weakly electric fishes, which have a highly developed electroreception system, have enormous cerebella (see Chapter 14) and associated neural systems. This results in very large relative brain weights for this family of fishes. The largest of these have brain weights that would be expected in birds or mammals of similar body weight.

Criticisms of Brain Allometry. Allometric analyses of brain and body development have been criticized on several accounts. First, the selective pressures that determine body weight are different for animals that have adapted to different types of environments. For example, vertebrates that fly, such as birds and bats, have a heavy selective pressure on them to reduce body weight in the interests of efficient utilization of energy. One of the ways birds have accomplished this has been by the development of a very light, porous bone structure. Similarly, vertebrates that live totally or largely in an aquatic environment have far less pressure on them to keep body weight

to a minimum because of the buoyancy of their body masses in water. This is especially true of animals living in salt water. Thus, marine mammals, such as whales and porpoises, and some extinct marine reptiles, such as plesiosaurs, ichthyosaurs, and mosasaurs, were able to achieve enormous body weights.

On the other hand, selection pressures for brain development have not been uniform either. The brain is not a unitary organ; rather, it is a complex organization of separate but closely interacting organ systems. These systems have different functions and are each subject to quite different selective pressures. For example, the autonomic nervous system, which is largely concerned with the regulation of the body's internal environment, is affected by a very different set of selective pressures than is the visual system or the motor system, which controls fine movements of the digits in mammals. In fishes in which taste has reached an extraordinary level of development, such as carps and catfishes, the region of the medulla into which the taste nerves enter has undergone a high degree of growth and specialization. To give one further example, in birds, many of which are highly specialized for vision, the optic tectum of the midbrain has reached a degree of size and complexity that is unrivaled in any other class of vertebrates. Thus, the variability in body-weight selective pressures seems to be matched by a comparable variability in brain-weight selective pressures. Nevertheless, even if these problems of variability may limit the mathematical power of allometric analysis, the type of plot that is shown in Figure 5-9 offers an opportunity to see the range of variation in brain size that can be found for a given body weight as well as the variation in body weight that can be found for a given brain weight.

Brain Size and Neuronal Organization. At the neuronal level, the specific effects of adaptations for larger and more complex brains are increased numbers of neurons and a more extensive dendritic organization, thereby permitting greater numbers of terminals to contact an individual dendrite. These changes allow greater precision and greater elaboration of interneuronal relationships. Selective pressures have favored more efficient packing arrangements so that the more elaborate neuronal systems have not resulted in an excessively enlarged head. These more efficient packing and processing arrangements include:

- Gathering of scattered neurons into more dense aggregations.
- Segregation of myelinated axons of the Golgi Type I neurons from other axons and cell bodies so that the neuronal mass is encapsulated within the white-matter tracts formed by myelinated axons.
- Subdivision of the neuronal mass into specialized components with different sources of input or different output destinations.
- Specialized arrangements of local circuitry, such as **lamination**, which is the organization of the cell and fiber constituents of a neuronal mass into separate layers of cells and fibers.

Within a laminar organization, such as the cerebral cortex, **local-circuit** arrangements arise that are orthogonal to the

BOX 5-1. Did the Dinosaurs Have Small Brains?

Many of our ideas about relative brain size and its importance for behavior are derived from the period between the 1880s and the early 1920s. This was a period of intense activity in paleontology. A number of paleontologists of this period were interested in brain evolution as it was reflected in the size and shape of the cranium, which is the bony container of the brain. Among their observations was the finding that the cranial capacities of huge dinosaurs, such as *Brontosaurus* and *Stegosaurus*, were relatively small in contrast to the great size and weight of the animals' bodies. Thus came into being the notion that the dinosaurs had small brains along with the implication that these animals must not have been very intelligent.

Harry Jerison has studied casts made from the interior of the skulls of dinosaur fossils. These casts, of plaster or plastic, are reasonably faithful indicators of the overall size and shape of the brain, as well as reproducing some of the finer surface details. Combining his estimates of the dinosaurs' brain volumes with paleontological estimates of the weight during life of the whole dinosaurs, Jerison was able to plot allometric polygons similar to those in Figures 5-9 and 5-10.

Figure 1 shows a dinosaur polygon plotted along with the polygons of living mammals, reptiles, and birds from Figure 5-9. The plot reveals three interesting features. The

first is that dinosaurs did indeed have brains that were very much smaller than would be expected for mammals or birds of equivalent body weight. The second is that even though the dinosaurs' brains were smaller than those of equivalent weight mammals, they were exactly what would be expected for reptiles of those body weights based on data from living reptiles. The dinosaur polygon thus appears to be merely an extension of the reptile polygon to greater body weights.

The third point has to do with *Archaeopteryx*, the presumed ancestor of all birds, which is represented as a filled black circle at the lower boundary of the bird polygon. The allometric relationship between its brain weight and the estimate of its body weight place it just within the bird polygon.

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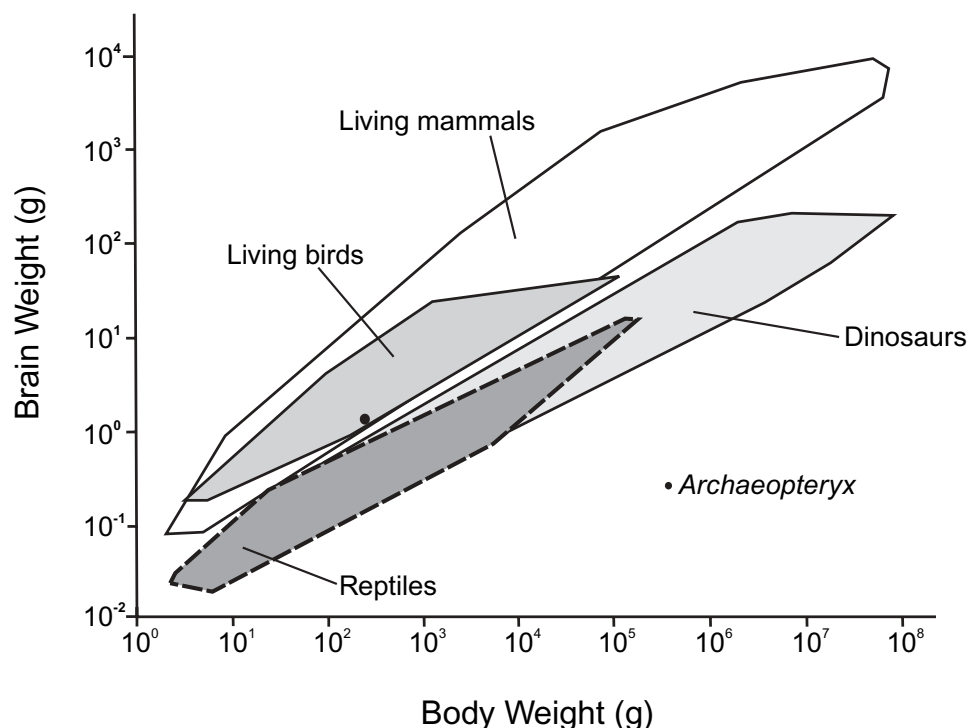


FIGURE 1. The brains of dinosaurs have been plotted in the same brain weight-body weight coordinate space as the brains of living mammals, reptiles and birds. Although dinosaurs had brain weights that were considerably smaller than those of mammals of equivalent body weights, they have brain weights that would be expected for reptiles of those body proportions. The filled circle at the lower border of the bird polygon indicates the brain weight-body weight relationship of *Archaeopteryx*, the presumed ancestor of modern birds. Adapted from Jerison (2001), with additional data supplied by Harry Jerison and used with permission of Spektrum Akademischer Verlag.

BOX 5-2. A New Taxonomic Method Based on Brain Allometry

Taxonomic classification typically has been based on the study of skeletal features because they provide a common basis by which to compare both living and extinct specimens. Analysis of genetic material has also proven to be a powerful technique for determining the classification and relatedness of species. Recently, Michel Thireau, Jean-Christophe Doré, and their colleagues proposed a method based on a statistical analysis of the brain. They call their method **neurotaxonomy**.

The method is based on an index derived from the intercept of the regression line of the allometric relationship between log brain weight and log body weight. The index is calculated from five brain regions: telencephalon, diencephalon, mesencephalon, cerebellum, and hindbrain. Within the telencephalon, further subdivisions provide an additional 20 indicators of "telencephalization." This aggregation of indices provides a unique brain "signature" for each species or subspecies studied.

By using a statistical technique known as factor analysis, the various species and subspecies can be sorted out into a matrix or factorial map from which the degree of relatedness can be determined. The method has been applied to amphibians, where it has successfully distinguished between two families of urodeles, the *Plethodontidae* (New World salamanders) and the *Salamandridae* (Old World salamanders), and to bats, insectivores (now called eulipotyphlans—see Chapter 4), and primates with similarly successful results. This method appears to be a useful way to separate closely related species that have many similar body features by analyzing their unique patterns of morphological differences within the brain.

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plane of lamination, that is, they cut across the laminae at right angles to form a **columnar organization** of cells and fibers. Laminar architecture appears to be a highly sophisticated form of neuronal organization. It often is found as the neural substrate of highly complex behavioral processes. It may not be the only form of neural organization that can support complex processing, however. As will be discussed in Chapter 25, birds exhibit many complex cognitive abilities, yet their telencephalons lack the six-layered, columnar structure of mammalian neocortex.

Selective pressures have also acted on variations in the molecular structure of the chemical messengers and modulators and on their neuronal receptors as well. Such adaptations, however, would not be expected to add substantially to either the weight or volume of the brain or of its individual gross components.

The Relative Size of the Neocortex. The neocortex of mammals often is regarded as the pinnacle of evolutionary

development of the brain. Although some of this notion derives from *scala naturae* thinking, mammalian neocortex does fit many of the criteria for a highly sophisticated brain structure—lamination, columnar organization, well developed local circuitry, and so on. Do humans have an exceptionally well-developed neocortex compared with other mammals or other primates? Figure 5-11, which shows data reported by Michel A. Hofman, suggests that they do not. The figure shows a regression plot of cortical thickness as a function of total brain volume for 22 species of mammals, of which a few selected examples are plotted. The figure indicates that human cortical thickness is precisely where it should be for a brain of that size. Because the human brain also is the appropriate size for its body mass, we can conclude that the relative thickness of the human neocortex is no greater than would be expected for a mammal of that body weight.

Also plotted in this figure are data from four species of cetaceans (whales and porpoises). These marine mammals have brains that are quite large in absolute size. The figure indicates,

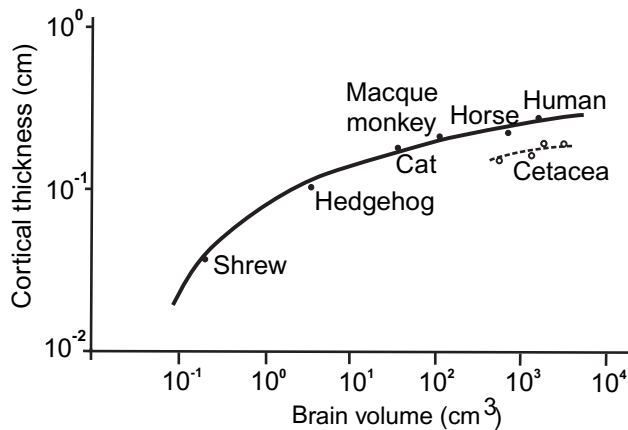


FIGURE 5-11. Cortical thickness as a function of brain volume for 22 species of terrestrial vertebrates. The data for only six individual species have been plotted. Also shown is a plot of cortical thickness of 4 cetaceans (whales and porpoises). Although among the largest of mammalian brains, both absolutely and relative to brain volume, the cetacean brains have markedly thinner cortical sheets than the terrestrial mammals. Adapted from Hofman (2001b) and used with permission of Spektrum Akademischer Verlag.

however, that the cetacean cortex is considerably thinner than that of terrestrial mammals of equivalent brain volume. Even though much has been made in the popular literature of the implications for intellectual capacities based on the large brain size in these animals, the figure reveals that the cetacean cortex has the equivalent thickness of mammals with brain volumes that are smaller by 1–2 orders of magnitude.

A cortical region that gets much attention for its supposed expansion in humans and other primates is the prefrontal cortex, which has been implicated in working memory, planning, social adeptness, and other high level cognitive functions. Figure 5-12 shows a plot of the volume of the prefrontal cortex in five species of mammals, including humans, as a function of total brain volume. Although humans surely have the largest volume of prefrontal cortex of any of the animals plotted, and probably of any mammal, the human data fall precisely on the regression line, which indicates that they have no greater volume of prefrontal cortex than would be expected for a brain of their size.

Domestication and Brain Size. In addition to changing by the process of natural selection, brains also can change due to specific human intervention—artificial selection, or selective breeding. Humans have been selectively breeding animals for the benefit of humans for thousands of years. The effects of these efforts on the various breeds and/or varieties of dogs, horses, chickens, pigs, cattle, fur-bearing animals, and so on are well known. Although the human interest generally has been in the production of eggs, milk, meat, wool, and other agricultural commodities, as well as speedier and stronger horses, dogs to serve various work and show purposes, and so on, this artificial selection also has had an inadvertent influence on the size of the brain and its component parts. The size of the telencephalon and its constituent regions appear to be particularly

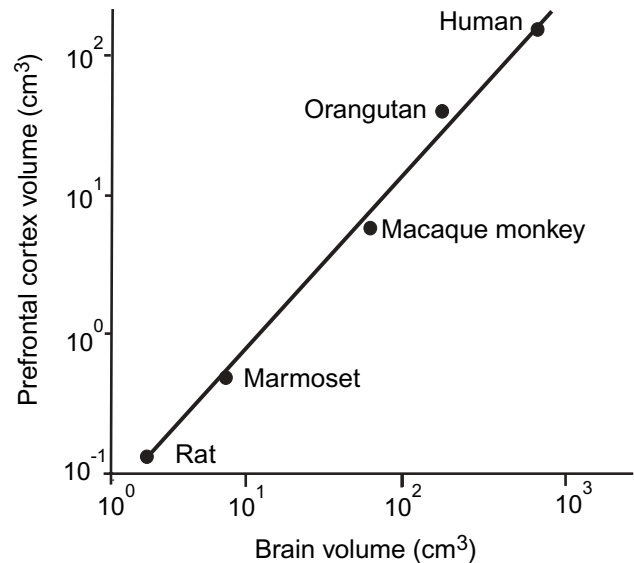


FIGURE 5-12. The volume of prefrontal cortex has been plotted as a function of brain volume for five species of mammals. Humans have the volume of prefrontal cortex that would be expected for their brain size. Data from Harry Jerison.

sensitive to the effects of domestication in both mammals and birds. In mammals, the auditory, visual, and motor cortices specifically are affected by domestication. In birds, the sensory regions of the telencephalon likewise undergo change. In all of these instances, the direction of change in the domesticated species is downward in comparison to their wild counterparts. The cause of this consistent change is not clear. Moreover, in those domesticated strains that have been specifically bred for their ability to socialize with humans, or to perform specific behavioral tasks, such as sheep herding or rat catching, their diminished brain size appears not to have interfered with their domestically and sometimes commercially valuable abilities.

BRAIN SIZE AND BEHAVIORAL ADAPTATION

Even though constraints on brain growth exist (see Box 5-3), the data nevertheless suggest a selective pressure for progressively larger brains, or at least for a progressive increase in certain brain components. For example, among mammals, sensory and motor areas of neocortex and other brain regions are larger in those that make extensive use of these sensory and sensory/motor systems. Why should this be so? Many paleontologists believe that behavior plays an important role in an animal's adaptation to its environment. Brain components have evolved in ways that are appropriate to the animal's behavioral adaptations. Those organisms with more numerous and more complex neural networks in certain systems have increased opportunities to survive. These superior neural control and processing systems permit enhanced sensory capacity to better detect more subtle changes and differences in the environment. Improved motor control permits better locomotion

BOX 5-3. Are There Constraints on Brain Growth?

Another interesting observation in Figure 5-11 is the effective range in which brain volume affects cortical thickness. Although the range of brain volumes in this data set varies across nearly five orders of magnitude, the range of cortical thickness varies over less than one order of magnitude. Hofman concluded from this that, among mammals, evolutionary changes have affected cortical structure in the horizontal dimension (parallel to the cortical surface) but not substantially in the vertical dimension (orthogonal to the cortical surface). If this is the result of a constraint on vertical expansion, it may account for the multiplicity of representations of visual space and sensory and motor representations of the body surface that have been reported in the cortex and that will be described in subsequent chapters. Indeed, telencephalic volume may have increased in response to a selective pressure for a cortical sheet with a greater area because greater thickness was constrained.

Other constraints on growth are limits on energy utilization and limits on neural processing capabilities. The more serious of the two are the neural processing limits, which require shorter and shorter conduction times and

processing times in order to achieve greater and greater size. This, in turn, would require more and more modularization. A number of neuroscientists, including Hofman, believe that we are probably close to the limits of brain size for humans.

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through the environment for predation, escape, territorial defense, reproduction, and so on, as well as more sophisticated manipulation of objects. Expanded integrative systems permit more information to be filtered, encoded, stored, and retrieved, which permits the animals to make greater use of their previous experience. Moreover, in the presence of certain specific stimuli, entire behavioral sequences have emerged that have important social consequences for territorial establishment and defense, courtship and reproduction, rearing of the young, feeding, and social organization.

Thus, while animals with less complexly organized, relatively smaller brains continue to survive, animals with larger and more complex brains have also been selected for. Basically, larger and more complex brains allow for the occupation of new niches. The diversity of the range of brain sizes and degree of complexity is thus a direct function of the diversity of potential new niches. The evolution of species with larger brains is in fact a reflection of an increase in diversity, which is limited only by the availability of new niches. That an increase in diversity—rather than a unilinear increase in brain size per se—has occurred among vertebrates is demonstrated by the trends for reduction and simplification in the central nervous system of some vertebrate groups. Amphibians are a prime example. The niches that such species occupy are as compatible with a reduced, simplified brain organization as other niches are with an enlarged, complex brain organization.

Brain Size and Intelligence

We have all heard the term “bird brain” used to suggest that someone’s intellectual capabilities are rather low. In contrast, terms like “big brain” or “brainy” suggest a person who is well endowed with the capacity to absorb large amounts of infor-

mation and to organize and utilize this information in creative and resourceful ways. Is this really the case? Does the size of a person’s brain give an indication of their intellectual ability? Are animals with smaller brains less intelligent than animals with bigger brains? Has evolution been progressively shaping larger brains in some lineages?

Early Views of the Evolution of the Brain and Intelligence. One of the early pioneers in the field of paleoneurology (the study of ancient brains) was Othniel Charles Marsh. Marsh was an eminent paleoneurologist and discoverer of many important fossil finds in the American southwest. He was interested in the sizes of fossil brains and what they could reveal about brain evolution. In the material that he studied, he observed what appeared to him to be certain trends in the history of brain evolution. These observations led him to propose several “laws” of brain evolution. These laws had a major impact on the thinking of comparative neuroanatomists of his era, and a number of his ideas became incorporated into their own speculations about the history of brain evolution among vertebrates. Marsh intended his laws as a description of evolutionary trends within the amniotes, but his ideas appear to have been generalized by others to the anamniotes as well.

The most general of Marsh’s laws states that, as evolution progressed toward the modern era, brains tended to increase in size relative to the body. Another law stated that this increase was mainly reflected in the cerebrum. Still another law postulated that, in some groups of mammals, evolution has produced a progressive increase in the complexity of cerebral convolutions.

The late Victorian era was also the period in which comparative psychology was developing the principles that would guide it, rightly or wrongly, for the next half century. One of

these principles was that intelligence and the capacity for behavioral complexity increase as animals “ascend the phylogenetic scale.” This principle seemed to fit in rather well with Marsh’s laws. In their view, as evolution “advanced,” nonhuman animals acquired relatively larger, more complex, more human-like brains, which made them progressively more intelligent, that is, more human-like in their activities. The seeming reasonableness of a parallel progression between brain development and intellectual development that advanced from simple to complex has kept these notions alive until very recent times.

Recent studies of relative brain size and comparative behavior in different lineages have led to some conclusions about brain size and intelligence that are rather different from the common sense model. In light of present day investigations, Marsh’s laws generally have come out rather well if their

application is limited to the groups for which they were intended, namely, the amniotes. They do not, however, tell the complete story.

Evolution of Intelligence. At the time that Marsh was making efforts to reconstruct the history of amniote brain evolution, similar efforts were under way by psychologists interested in reconstructing intellectual evolution. In 1882, George J. Romanes published a book entitled *Animal Intelligence*, which was the first attempt of the modern era at a scientific analysis of the subject. In Romanes’ conception, intelligence was the capacity of an animal to adjust its behavior in accordance with changing conditions. For Romanes, the hallmarks of intelligent behavior were “conscious choice” and “intentional adaptation.”

BOX 5-4. Brain Evolution and Consciousness

While this book is first and foremost a book on comparative neuroanatomy, we wish to add here a brief digression on comparative behavior and consciousness. Just as neuroanatomical theories of brain evolution must be reevaluated and revised as new information becomes available, so too must the theoretical foundation for behavioral studies. One tenet of such studies that has been long accepted is that put forward by Conway Lloyd Morgan, who was a comparative psychologist of the Victorian era. Lloyd Morgan had a profound influence, extending to the present time, on how animal behavior is viewed.

A contemporary of Romanes, Lloyd Morgan was the author of two influential works, *Introduction to Comparative Psychology* (1894) and *Animal Behaviour* (1900). Lloyd Morgan’s ideas were in the tradition of nineteenth century “faculty psychology,” which held that the human mind was composed of various faculties or powers, among which were perception, memory, judgment, self-esteem, and so on. Humans shared the lower faculties with some other animals, but the highest were exclusively human. Lloyd Morgan, however, was greatly concerned about the then prevalent custom of “anthropomorphism,” which was the attribution of the full range of human faculties to non-human animals. He summarized his views in his famous Canon: “In no case may we interpret an action as an outcome of the exercise of a higher psychical faculty, if it can be interpreted as the outcome of one which stands lower in the psychological scale.” Thus, we should not assume that nonhuman animal behavior is the result of complex, human-like processes if the behavior can just as well be explained by simpler mechanisms. In other words, you should not assume that your pet dog is showing love for you by licking the back of your hand; the dog just may be enjoying the salty taste of your perspiration.

Lloyd Morgan’s Canon maintained an influence on our ideas about the evolution of animal intelligence and its relation to the evolution of the brain that still can be felt today.

Its suggestion of a progressive scale of intellectual development, however, was a natural companion to the progressive scale of brain development that Marsh’s laws seemed to suggest. Lloyd Morgan added a cautionary note to the Canon: “To this it may be added—lest the range of the principle be misunderstood—that the canon by no means excludes the interpretation of a particular act as the outcome of higher mental processes, if we already have independent evidence of their occurrence in the agent.” Despite this caution, the basic idea that animal consciousness is limited to simple sensory perception with only the most basic of ideas that are restricted to the immediate situation and serve merely to prompt or guide an action has become all but enshrined in the discipline of psychology. Its corollary, that humans have singular attributes of language and higher cognitive processes such as thought, episodic memory, and reasoning, is likewise not only widely accepted but vigorously defended by some.

Lloyd Morgan did a great service to the advancement of the discipline, which was needed in the atmosphere of the time. In those days, all animal behavior knowledge was from anecdotes, fairy tales, and tall stories. Relatively little serious research on animal behavior was carried out until after World War I. For the development of this area, rigorous assessments of animal behavior benefited by eliminating all of the then unfounded attributions of human characteristics to animals. Lloyd Morgan’s position strongly argued against attributing such human abstractions to animals, such as “honor,” as was popularly done by Victorian writers.

Lloyd Morgan probably did not believe that any animals had cognitive abilities, however, a view that recently has received wide acceptance among animal behaviorists, for at least some mammals and birds. Thus, his points need to be reexamined in this context. Anthropomorphization may remain a hazard to clear thinking in scientific work; however, the denial of any shared, higher cognitive func-

BOX 5-4. Brain Evolution and Consciousness—cont'd

tions is just as surely to be avoided. A priori denial of higher cognitive abilities to nonhuman animals is as attractive and comforting a trap as is the *scala naturae*. What is important to remember about Lloyd Morgan's caution is that his Canon does not exclude the assignment of higher mental processes to nonhuman animals *if independent evidence exists for them* [our italics]. The studies of the past several decades, including studies of complex cognitive and language abilities in chimpanzees and other great apes, as well as in some species of birds, supply the required independent, objective evidence of higher mental processes.

A further point is that of parsimony. The dictum of parsimony (see Chapter 1) is recognized as applicable to most areas of science. In studies of comparative cognition, however, it is ignored and instead superseded by Lloyd Morgan's Canon. From the argument of parsimony, one might argue for the reverse of the Canon and state in its place: *If the behavior of an animal in a particular setting is similar to the behavior of a human in the same setting, one should at least consider the possibility that similar mental processes may have produced it.*

As we learn more and more about the evolution of brain structure and in parallel learn more and more about the cognitive abilities of at least some nonhuman animals,

we will achieve a new and more realistic perspective on the mind and its evolution. The contribution that comparative neuroanatomy has to make to understanding the neural bases of cognitive processes is enormous and just at the threshold of being tapped. Many animals with large brain-body ratios exhibit complex cognitive abilities, which we then associate with "consciousness," however that challenging word and concept is defined. On the other hand, it is equally important to posit that the absence of complex cognitive behavior does not by any means rule out the possible presence of consciousness.

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What Is Intelligence?

What is intelligence and how can we determine its presence or absence in animals? Intelligence is a term that has been applied to human behavior in a wide variety of ways. A common feature of many definitions of intelligence is the notion of a purposeful adaptive behavioral response to the demands of the environment. Intelligence theorists argue at length about whether intelligence is a general characteristic of an organism that is applicable to many diverse situations, whether it is merely the sum of a number of rather specific abilities, or some combination of both. Whatever the definition of human intelligence, an important consideration in applying it to other animals is that intelligence is not a biological property of organisms, such as height, cranial volume, or cortical surface area. It is a value judgment on the part of the observer about the merits of the behavior observed. The intelligence tester decides which behaviors are important to measure. If the subject, whether human or other animal, performs those behaviors well, the tester concludes that the subject is very intelligent. Poor performance on the test results in a rating of low intelligence. In a different culture, however, a very different set of behaviors might be rated as "intelligent."

The same cautions apply in the assessment of nonhuman animal intelligence. In their desire to compare nonhuman animal intelligence to human intelligence, comparative psychologists generally have sought to measure the performance of their subjects in behavioral situations that humans value.

Moreover, they have tried to make the tests as similar to human tests as possible to facilitate the comparison. In many cases, the tests have built-in biases similar to the cultural biases in the human tests. For example, rats frequently do poorly on most tests intended to assess their intelligence. These tests, however, almost invariably involve visual stimuli. Vision is a very important distance sense for humans and other primates, but it is much less important for nocturnal animals. The senses of smell and hearing are considerably more useful distance senses for such animals. Indeed, when given a test of behavioral adaptability that uses olfaction rather than vision, rats perform as well as many primates do on visual tests. When attempting to characterize the intelligence of nonhuman animals, we should make every effort to test them in ways that are appropriate to their own mode of life.

We should not view nonhuman animal intelligence as a scaled-down version of human intelligence. To do so would fail to take into account the unique adaptations of nonhuman animals and would ignore the very special nature of human intelligence. Human intelligence is different from nonhuman animal intelligence in any situation in which our capacity for language can be applied. First, we can communicate with others in a rich and complex way. Second, we cannot only communicate with the present, but with the past and with the future by means of language. Very few nonhuman animals have the ability to pass on the benefits of their experiences to multiple generations. Third, the ability to formulate a problem and its solution in linguistic form provides us with reasoning

capabilities that are well beyond the reach of any nonhuman animal. If you say to yourself “two lefts, one right, one left, and two rights” you have an enormous advantage over a nonhuman animal in attempting to learn the correct path through a maze.

Intelligence and Brain Size. In general, the greater the degree to which a psychological capacity is developed, the greater is the amount of neural tissue that is devoted to processing that capacity. Jerison referred to this relationship as the **principle of proper mass**, and we will see many illustrations of this principle in this book. If follows from this relationship that those parts of the brain that process intellectual information should be larger in animals that do a lot of such processing (i.e., are more intelligent) than in those that do less processing. Investigators of this problem are aware that large amounts of the brain are not devoted to intellectual activities but rather are involved in the “vegetative” or visceral aspects of being alive, as well as operating the musculoskeletal system. To separate intellectual from visceral and musculoskeletal functions, investigators have examined the ratio of brain weight to body weight or brain weight to spinal cord weight. By this reasoning, brains that are larger than average for a given body or spinal cord weight must be performing additional nonvisceral and nonmusculoskeletal processing.

The assumption has been that this other neural processing represents the intellectual activities of the brain. This, in our view, is somewhat of an oversimplification. Included in the nonmusculoskeletal and nonvisceral functions are arousal, wakefulness, and attention, emotion, and sensory processing, as well as the work of major integrative and coordinating systems such as the cerebellum and the limbic system; some of these are involved in intellectual activities, and some are not. Some investigators have attempted to deal with this aspect of the problem by studying the weight or volume of the neocortex of the brain in mammals as a proportion of total brain weight or volume. Because intellectual functions also involve regions other than the neocortex, this approach is not completely satisfactory either. Likewise, the regions that involve complex cognitive processes in nonmammals, such as birds, include nonlaminated parts of the telencephalon and other regions as well. Identifying the necessary and sufficient neuroanatomical substrate for cognition and consciousness in any taxon has yet to be done.

One attempt to assess directly the merits of the notion that a big brain necessarily means big intelligence has been to examine the human data on brain size and measures of intelligence. The literature in this field contains some well-known examples of eminent persons whose brains have either been heavier than normal (supporting the view that “brainy” and “intelligent” should indeed be synonymous) or surprisingly small, which has been used to argue for the contrary position. Neither of these observations makes a useful contribution because brain weight decreases considerably in a person’s later years, and an elderly sage is likely to have a much lighter brain than one closer to middle age. Moreover, at any age, the longer a brain remains in the skull after death, the more it gains in weight due to the accumulation of body fluids (edema). These problems and others make many of the brain-weight values given for eminent persons of the past, such as Anatole France and Oliver Cromwell, rather suspect as indicators of the rela-

tionship between brain size and intellect. Contemporary studies of intelligence and brain size have found that the relationship is not strong at all.

Some of the allometric plots shown in this chapter have been used to make the case that relative brain size indicates relative intelligence. Thus, if two species of the same body weight have different brain weights, the one with the heavier brain weight is presumed to be the more intelligent. Put the other way around, the argument sounds less convincing: If two species have the same brain weight but different body weights, the one with the lesser body weight is presumed to be the more intelligent. In our judgment, the question of intelligence and brain size remains largely an open issue.

SUMMARY AND CONCLUSIONS

The comparative study of vertebrate nervous systems, whether from the perspective of anatomy, physiology, chemistry, or behavior, can be carried out in a phyletic context or in an adaptation context. Both approaches are equally valid. Moreover, data obtained from one approach often can aid in the interpretation of data from the other. Problems arise, however, when the goals of the two approaches are not kept clearly separated. The results of a study that is adaptational in character should not be taken to necessarily represent the historical course of evolution. Adaptation studies frequently organize results in a sequence of increasing complexity; this is not necessarily the course that was followed in the history of any lineage. Finally, concepts such as “progress” or “advancement” should be seen as highly dependent on a specific environment and not as absolutes. A sudden drastic change in environmental circumstances can quickly convert an adaptational success into an evolutionary disaster.

Behavioral adaptation involves many neural systems ranging from those that sense the environment and move the body to those that process and store information and make decisions. Intelligent behavior is one of the most sophisticated forms of adaptation to the environment. We must, however, look beyond relatively coarse indicators such as overall size or weight of the brain if we are to find anatomical correlates of intelligence. Moreover, we must not expect to find the same brain components necessarily to be correlates of intelligence in different taxonomic groups. The more closely related two species are or the more similar are their adaptations to the environment, the more likely we are to find a common substrate of intelligence. The points made in this chapter should be given consideration by the reader as we examine, in subsequent chapters, theories of how brains evolve and as we describe the structure of the subdivisions and component systems of the brains of vertebrates and their roles in behavioral adaptation to the environment.

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6

Theories of Brain Evolution

INTRODUCTION

The Darwin-Wallace theory of biological evolution is one of a handful of theories that can be said to have truly changed the way the world is viewed and the place of humans in it. Indeed, it is arguably the single most important theory in the history of biology. Unfortunately, not all biologists experience much formal education in evolutionary biology, and this lack often characterizes the training in the biomedical sciences, which include the neurosciences. Because of the importance of the theory, however, it is not at all unusual for a student of the brain to attempt to put the results of his/her research into some sort of “evolutionary” context or even to devise a theory of how the brain has evolved based on those findings. A number of such theories have been offered. Some have had no influence whatever in the field of comparative neuroscience, some have had influence in some form or other in the popular press, and some have been incorporated into the lore of neurobiology.

One of the most widely accepted of the earlier theories of brain evolution was that of C. Judson Herrick. Herrick’s career began at the turn of the century and continued for more than 50 years, although he was most active in the 1920s and 1930s. His ideas and those of his student, Elizabeth Crosby, dominated comparative neurology well into the 1960s. So influential was Herrick that some of his ideas have attained the status of dogma in comparative neuroanatomy.

Herrick believed that the evolution of nervous tissue was similar to its embryology in that the brains of ancestral vertebrates were undifferentiated tissue. A stabilization of this tissue into permanent structural patterns occurred during phylogeny.

He believed that with progressive increase in complexity of adjustment to the external and internal environments, a corresponding differentiation of structure occurred. Herrick further believed that the process of differentiation itself limits the future course of evolution within boundaries determined by the efficient working of the established organizational pattern. The result was an orthogenetic (i.e., proceeding in one direction), irreversible course of evolution of the nervous system. These ideas have been incorporated into most of the proposed theories of others:

- The ancestral vertebrate brain was diffuse and poorly differentiated.
- During evolutionary history, brains become more and more complex and, therefore, more differentiated.
- The course of evolution is essentially unidirectional and not reversible.

SOME COMMON ASSUMPTIONS

In Herrick’s defense, it should be stated that these ideas were not unique to him, but were a reflection of the views that were widespread in the biological and anthropological communities in the nineteenth and early twentieth centuries. As discussed in Chapter 1, these views were a result of an assumption of evolutionary progress, a product of combining Darwinism with the *scala naturae* theories of the mid-nineteenth century, and a pervasive anthropocentrism that continues to the present day. Since humans are supposedly the smartest creatures on the planet, the ideal brain must be like ours: large in size, complex,

and highly differentiated. Conversely, the ancestral vertebrate brain must be the opposite of this: small, simple, and undifferentiated. Supposedly then, during the course of evolution, brains have gone from small to large, simple to complex, and undifferentiated to differentiated. This was, and still is for many, the dogma. Good evidence exists, however, that most, if not all, of these assumptions are wrong. As a result of starting with these false assumptions, many of the conclusions that have flowed from them have likewise been wrong.

The tradition has been to choose the brain of a single animal as the exemplar of the ancestral brain. In the 1950s and early 1960s, biomedical scientists usually used the brain of the laboratory rat to represent the brain of a “primitive” mammal. More recently, the hedgehog, a member of a group of so-called “basal insectivores” (now Eulipotyphla—see Chapter 4) has become the exemplar, because it better fits the expectations cited above. Relative to the brains of other placental mammals, the brain of the hedgehog is small, seemingly simple, and relatively undifferentiated. Authors have frequently described it as **generalized**. Living eulipotyphlans may or may not retain more ancestral features than most other living placental mammals, and they have their own specializations and derived characters. These animals are mostly nocturnal and/or crepuscular. Consequently, their visual systems are probably secondarily reduced. As discussed in Chapter 4 (see Fig. 4-13), eulipotyphlans are most closely related to the groups of mammals that include hoofed mammals, cetaceans, carnivores, and bats, all of which constitute the outgroup to the taxon that includes primates, rodents, and lagomorphs (rabbits and the like). In fact, from a phylogenetic point of view, one could have as much expectation of finding “primitive” features in the brain of a porpoise, a horse, or a cat as one could have for the hedgehog. Features of the visual system and other parts of the brain in eulipotyphlans can only be identified as like that of ancestral mammals by out-group comparisons, as discussed in Chapter 1, not by finding features that fit preconceived notions. As shown in Figure 4-13, the outgroup to the two sister groups of the primates-rodents-lagomorphs taxon and the large taxon that includes the eulipotyphlans is a highly diverse assemblage that includes elephant shrews, aardvarks, hyraxes, manatees and dugongs, elephants, and tenrecs and golden moles. Very little information is available on brain structure for these animals.

Along with the belief that the brains of some extant species, such as hedgehogs among placental mammals, resemble ancestral mammals, another assumption has been that adult structures in the brains of these species are the homologues of embryonic structures in other mammalian species, such as primates. In other words, at least some of the features of the brain of a primate would be the result of the brain of a hedgehog undergoing further embryonic development. Both developmental and comparative studies have amassed a great deal of evidence against this notion, but these recapitulationist assumptions are persistent in the literature and form components of many theories of brain evolution. We will note a different viewpoint on the recapitulation question at the end of this chapter, which makes sense of the grain of truth in this otherwise misbegotten idea.

PREVIOUS THEORIES OF VERTEBRATE BRAIN EVOLUTION: ADDITION OF STRUCTURES OR AREAS

MacLean

A number of theories assume that if organisms develop new adaptations and functions, then new structures must have been added to already functioning brains. New structures may be added, of course, but old structures may be modified as well. In fact, modification of existing structures may be more common a process than addition in other organ systems. An example of an additive theory is Paul MacLean's **triune brain theory**, developed in the 1960s. MacLean postulated that the human brain is composed of a hierarchy of three formations: the R-complex (or reptilian complex), which comprises the basal ganglia; the paleomammalian brain, which comprises the limbic system; and the neomammalian brain, which consists of the dorsal thalamus and the neocortex (isocortex). This theory states that humans have inherited these three brains from their reptilian, early mammal, and late mammal ancestors, respectively, and that with the addition of each superimposed brain, new cognitive abilities and behaviors have appeared.

Although MacLean's theory has had no significant impact on neurobiology, it has become popular in the lay press and among some psychological and educational therapists, partially due to the publication of *Dragons of Eden* by Carl Sagan in 1977. The extensive body of work in comparative neurobiology over the past three decades unequivocally contradicts this theory. First, homologues of the limbic cortical areas that MacLean considers to have been first present in early mammals have been found in nonmammalian vertebrates. Second, homologues of neocortical structures and of dorsal thalamic nuclei also have been found in nonmammals. Third, MacLean's observations on the behavioral differences between mammals and nonmammals are oversimplified and ignore the elaborate social and parental behaviors of some nonmammalian vertebrates, including birds and a variety of ray-finned fishes.

Flechsigs and Campbell

Workers such as Paul Flechsigs and Alfred W. Campbell (in the late nineteenth to early twentieth centuries) thought that an orderly addition of cortical areas accompanies a progressive elaboration of sensory-motor processes in mammals with the more complexly organized brains. This idea has found a place among the beliefs of many in neuroscience. For example, Broca's area for speech in the neocortex has been considered to be unique to humans and not to be found in the brains of monkeys. Recent work has shown that a homologue of Broca's area is present in the brains of monkeys, although it apparently plays no role in vocal communication in these animals. Similarly, Norman Geschwind elaborated a theory that the inferior parietal lobule of the neocortex, an “association area of association areas” believed to be involved in language processing, was unique to humans. Once again, recent work has shown it to be present in monkeys as well.

Sanides

In the 1970s, Friedrich Sanides promulgated a view of regional cortical evolution that was the opposite of that commonly held. Most workers believed that the primary sensory areas, that is, those areas of the neocortex receiving direct projections from dorsal thalamic sensory nuclei, appear first in phylogeny, and that association areas of neocortex appear later in phylogeny in mammals with more complex brains. Sanides thought that the association areas are older and the primary areas newer. He inferred a sequential evolution of cortical areas in progressive waves of differentiation due to a trend toward increasing architectural specialization in the arrangement of cortical neurons, and believed that the trend culminated in the appearance of specialized primary sensory areas. Specialized primary sensory areas, however, are found in all mammals and in a great variety of nonmammals as well. This now discredited theory is a good example of why trends perceived by humans and based on human value scales (such as a greater versus a lesser degree of architectural organization) are perilous at best.

PREVIOUS THEORIES OF VERTEBRATE BRAIN ORGANIZATION: NEW FORMATION AND REORGANIZATION OF CIRCUITS

Herrick

Herrick put forth a specific theory on how the well-differentiated cerebral cortex of mammals has evolved. He held the view that in order to evolve well-differentiated cortex, well-defined tracts of projections from the dorsal thalamic sensory nuclei had to penetrate the telencephalon. These tracts would have to have different physiological properties, such as vision, audition, and somatic sensation. Herrick believed that fishes and amphibians lacked well-differentiated cortex because he thought that the entire forebrain was dominated by the olfactory sense, leaving no space for other modalities. Furthermore, no significant penetration by projection fibers of other modalities occurred in these groups of animals. Herrick thought that reptiles were the first group of vertebrates to possess a forebrain with some areas free of olfactory influence. He thought that thalamic sensory projection fibers began to make an appearance and that a rudimentary cortical formation was present in these groups. He considered birds to have gone off in an aberrant direction and to have developed no neocortical precursor, while in mammals most of the forebrain became a thalamic sensory projection target and only a small portion of it remained devoted to olfaction. The penetration of numerous thalamic projection fibers then supposedly allowed the development of six-layered neocortex. This scenario has been referred to by some as an **invasion hypothesis**.

Bishop

In 1959, George H. Bishop, a distinguished American neurophysiologist, described several generalizations bearing on the course of evolution of sensory systems in the brains and spinal

cords of vertebrates. The framework upon which these generalizations rested was a general principle of nervous system evolution derived from Herrick's 1948 classic book, *The Brain of the Tiger Salamander*, and referred to as **cephalization** (not encephalization). This concept embodies the idea that during the course of vertebrate evolution, successively higher level structures were added to the rostral portion of the brain in relation to the evolution of more rostral special sensory levels. This concept implied a progressive shift towards the rostral portion of the brain in the processing of sensory information. For example, the observation that some nonprimates were rendered apparently blind by lesions of the optic midbrain, while primates were not so affected until lesions were made in the visual part of the neocortex suggested that ultimate control of vision had shifted from the midbrain to the forebrain. This result was considered to support the concept of cephalization.

Bishop proposed that during the course of vertebrate evolution, as cephalization progressed, the extension of each spinal pathway related to different sensory systems occurred not only by the addition of synaptic links above the old terminus, but also by adding more and successively larger caliber fibers in parallel with the nerve fibers already supplying lower level functions. Within each ascending afferent system, the supposedly newer, larger fibers were believed to bypass the more caudal and supposedly older terminal sites in favor of projecting to the newer, more rostral sites. The belief that smaller caliber fibers were developed earlier in evolution than larger caliber ones was a generalization of this concept.

Ariëns Kappers

Cornelius Ubbo Ariëns Kappers was an important Dutch comparative neurologist of the early years of the twentieth century. He formulated a theory of **neurobiotaxis** that described a phenomenon that he believed to be a force for change during vertebrate evolution. The theory states that if several centers of stimulation of neurons are present, the outgrowth of the chief dendrites of those neurons and eventually their cell bodies shift in the direction of greatest stimulation, resulting in lengthening of the axons. This response was believed to occur only if the source of stimulation was functionally related to the affected neurons. Good evidence confirming the existence of neurobiotaxis has not been found, however, since Ariëns Kappers put forth this notion.

With **G. Carl Huber** and **Elizabeth Caroline Crosby**, Ariëns Kappers published a three-volume work, *The Comparative Anatomy of the Nervous System of Vertebrates, Including Man*, first published in 1936. This work stood for more than three decades as the authoritative and master reference for comparative neuroanatomy. Although a number of the hypotheses of brain evolution contained therein subsequently have been either discarded and/or illuminated and revised by new insights from histochemistry, electron microscopy, the newer tract tracing methods, and other advances, it remains a remarkable monument to the dedication and vision of its authors.

Bowsher

David Bowsher, a British neuroanatomist, presented a "theory of the phylogenetic progression of central sensory

systems" in 1973. Bowsher was greatly influenced by the theory of neurobiotaxis and used it to explain a number of observations on the topography of nuclear groups. He was also influenced by the works of **Ramon-Moliner** and **Nauta** in 1966 and Ramon-Moliner in 1968, in which the central reticular core of the mammalian neuraxis is described as being composed of neurons with a presumably primitive, simple dendritic morphology referred to as **isodendritic**. The morphology of these neurons was considered to be primitive because similar neurons were believed to make up almost the whole neuraxis of jawless vertebrates and cartilaginous fishes. These animals have been presumed by many neuroanatomists to be primitive types of living animals that can be used to represent ancestral vertebrates. Ramon-Moliner considered these isodendritic neurons to be a kind of cell from which many more elaborate types of neurons could be derived. Bowsher considered the primitive vertebrate nervous system to resemble a reticular nerve net in which each individual primitive cell would be synaptically connected with many other neurons. His opinion is at least partly based on a comment by Herrick that the neuraxis of amphibians is essentially a nerve net.

Bowsher believed phylogeny to be an "historical antero-grade progression," and his theory was intended to answer the question of how specific, lemniscal (distantly projecting) systems evolved from a presumably primitive, reticular-like system. He believed that the earliest specific centers to appear were also composed of isodendritic neurons that were "captured" by a set of homogeneous afferent fibers carrying a single kind of sensory information. Several nuclei in the hindbrain of mammals—the nucleus of the solitary tract, which is involved in the taste system, and the vestibular nuclei, which are involved in balance and equilibrium—were given as examples of this earliest step in the march toward specificity. The next postulated stage was the induction of some morphological specialization in the central neurons receiving ascending branches of primary afferent sensory fibers. These newly evolved specific centers were believed to send projections to the isodendritic neurons of the reticular core but not to receive projections from them. Bowsher considered the principle (sensory) nucleus of the trigeminal nerve (that supplies the face) to be the first such nucleus to appear in phylogeny. To explain the existence of both isodendritic primitive neurons as well as specialized ones in many mammalian thalamic nuclei, Bowsher suggested that the efferent projections of newly evolved centers, such as the principal trigeminal nucleus and the dorsal column nuclei (that relay somatic sensation from the body), invade an originally isodendritic thalamus and trigger the differentiation of the complex neurons that become thalamocortical relay cells. When the process of specific "takeover" is incomplete, such nuclei still have reticular as well as specific sensory afferents, and thus both types of cells. Bowsher also indicated that the number of inhibitory Golgi type II interneurons increases "with the phylogenetic progression."

Diamond and Hall

In 1969, Irving Diamond and William Hall proposed a specific hypothesis of the course of evolution of the central visual system in the primate lineage as a part of an essay on the evolution of primate neocortex. They inferred the existence of four

evolutionary stages. Three of these stages were represented by the central visual pathways of three living groups of animals, and the earliest stage by a hypothetical construct (a reptile-like mammal). The sequence of stages was reptile-like construct, tree shrew, prosimian primate, and anthropoid primate. In the first stage, the eye was believed to project only to the optic tectum of the midbrain, which in turn would project to an undifferentiated thalamic visual nucleus. This nucleus would then project to a general sensory cortex. The second stage was believed to be one in which the single thalamic nucleus has split into two, one receiving input from the eye directly and the other receiving visual input relayed through the optic tectum. These two thalamic nuclei then would project to a visual cortex differentiated into a visual "core" cortex and a surrounding belt of association cortex with both nuclei projecting to both cortices. In the third and fourth stages, progressive differentiation and separation of the two pathways to visual cortex and of the cortex itself were believed to have occurred. Serious doubt has been cast on this theory by more recent studies of visual pathways in many nonmammalian vertebrates, demonstrating that nonmammals also have multiple, separate visual pathways. Nonetheless, serious questions on the evolution of the visual and other sensory systems across amniotes still persist, as discussed below. The recognition by Diamond and Hall of the significance of the tectal and thalamic sensory components for illuminating the evolution of these systems was one of fundamental importance.

CRITIQUE OF PREVIOUS THEORIES OF VERTEBRATE BRAIN EVOLUTION

Detailed critiques of the evidence for and against each of these theories are not appropriate here. Examining the underlying assumptions that form the conceptual framework for them may be worthwhile, however. First, some of these workers have an anthropocentric, *scala naturae* view of the animal kingdom. They refer to it as the **phylogenetic progression** or the **phylogenetic scale** or use other similar names. This fallacy is particularly apparent in the writings of Herrick, Bishop, and Bowsher. Second, most of these workers tend to view the course of evolution of whatever system is being examined as a progression of one kind of change from a simple to a complex condition. This progression is viewed as occurring in step with the ascent up the phylogenetic scale. Homoplasy, particularly parallelism and convergence, are not considered as factors in evolution. This unidimensional progression, seemingly under the direction of some imperative, is reminiscent of the now discredited, "predetermined path" theory of apparent steady lines of "progressive" evolution or a trend in one definite direction, referred to as **orthogenesis**.

Clearly, most of these workers have been greatly influenced by Herrick. If we remember the years during which this outstanding neurobiologist was most active and consider that notions of orthogenetic evolution, evolution in one direction, that is, from simple to complex states, and the *scala naturae* were common in biological thinking at that time, it is not difficult to understand how he came to these views. For example, in 1896, Edward Drinker Cope, the American paleontologist,

inferred a **law of the unspecialized**, whereby phylogenetic sequences lead from generalized, primitive forms to more and more specialized forms. Since superficial observation often appears to confirm this notion, and indeed it is sometimes true by chance, this idea has been influential. G. H. Eimer introduced the concept of orthogenesis in 1888. These trends were thought to demonstrate a “directed” evolution.

An assault was made on the concept of orthogenesis by the leading neo-Darwinians, especially Glenn Jepsen and George Gaylord Simpson, in the 1940s and 1950s. A considerable amount of contrary evidence was gathered, and some of the most famous examples of orthogenesis were refuted. Orthogenesis is mentioned in contemporary evolutionary works only as an historical curiosity. Nevertheless, the application of the concept still appears in the work of some comparative neuroanatomists.

Most of the theories described above imply a progression from a simple condition—usually an undifferentiated structure—to a structure divided into subdivisions or parcels. Surely such a sequence does often occur; however, to construct a theory in which only such a sequence is possible is to ignore a significant body of evidence. Evolution does not always produce a progression from simple to complex. Many examples exist where features evolve from complex states to simple ones.

Another problem with many of the theories is that ancestral states are often inferred by using inappropriate comparisons or models. Most often “primitive survivors” are used to infer what the ancestral state was—usually jawless vertebrates and elasmobranchs for vertebrates and hedgehogs for mammals. Neither jawless vertebrates nor elasmobranchs, within each group of which occurs a marked range of variation in brain structure and degree of complexity, can be considered to represent ancestors of extant amphibians or extant amniote vertebrates, however. As noted above, hedgehogs are equally useless as a model of mammalian ancestors.

PARCELLATION THEORY

Ebbesson

Sven O. E. Ebbesson, a Swedish-American neuroscientist, published a **parcellation theory** of brain evolution in 1980 that rejected invasion hypotheses such as those of Herrick and Bowsher. Ebbesson proposed two main ideas. First, he proposed that ancestral vertebrate brains consisted of diffuse, relatively undifferentiated systems. These undifferentiated brains, nevertheless, had more extensive fiber connections with more overlap than is seen in living vertebrates. Second, he proposed that nervous systems have evolved from a simpler, more diffuse condition to a more complex condition by the parcellation of cell populations into subdivisions, brought about by the segregation of inputs, competition of inputs, and the loss of some connections. Ebbesson contended that abnormal connections seen in plasticity experiments represent ancient connections that were lost in modern organisms. The idea that early vertebrate brains were diffuse, undifferentiated, and containing only widely interconnected parts is in accord with the ideas of Herrick, Bowsher, and Diamond and Hall.

While the basic idea of diffuse to specific may be an oversimplification, over the past several two decades, more and more examples of parcellation have been identified, and this theory is gaining significant credence. Evolution of the dorsal thalamus among tetrapods is a prime example: a single rostral nucleus in the dorsal thalamus of amphibians appears to be the homologue of three or more nuclei in reptiles, five to ten nuclei in birds, and at least five nuclear groups in mammals, most of which comprise three or more individual nuclei. Multiple nuclei in the caudal part of the dorsal thalamus and their multiple subdivisions may also have evolved, at least in part, by a process of parcellation. Other processes have contributed to dorsal thalamic evolution as well, involving the gain of a number of new ascending pathways and other connections, but the parcellation process appears to have contributed significantly. Changes in the proliferation and migration patterns during embryological development, as discussed in Chapter 3, would be expected to supply at least part of the underlying mechanism for parcellation phenomena.

Deacon

Additional theories relating to evolution from a developmental perspective have been proposed, such as the **displacement hypothesis** of Terrence Deacon. Deacon argued that where changes in connections occur over evolution—the loss of connections, acquisition of additional connections, or replacement of one class of connections by another—competitive axonal interactions are biased by contextual events during development. He believes that this mechanism can explain invasion-like and parcellation-like events. He considers a cause to be missing from both invasion and parcellation hypotheses, whereas he believes his displacement hypothesis presents a mechanism of change. The cause is in the form of regressive processes, for example, cell death or reduction of a peripheral sensory or motor system, or differential growth processes.

CURRENT THEORIES OF FOREBRAIN EVOLUTION

Forebrain Evolution: Experimental Foundations

In the earlier part of this century, the predominant school of thought on forebrain evolution had held three major tenets. First, while the neocortex of mammals had long been recognized to be the site of many of the so-called “higher” mental functions, only a small part of the more simply organized cortex in reptiles had been thought to be a “precursor” for the neocortex, and no potential homologues for it were thought to exist in anamniote vertebrates. Second, the telencephalons of the earliest vertebrates and of extant anamniotes were thought to be dominated by a massive olfactory input to the exclusion of other sensory system projections. Third, the *scala naturae* approach to evolution dictated a unilinear, progressive history of brain evolution. Beginning in the late 1960s, new findings on the organization of sensory system pathways and the telencephalon formed the basis for a new comparative anatomical approach to brain evolution that avoided the biases and pitfalls of the *scala naturae* and progressionism.

Part of the foundation for the comparative studies on reptiles, birds, amphibians, and fishes was the ground-breaking set of discoveries about how the various ascending sensory systems are organized in mammals. In the decade of the 1960s and previously, only one visual pathway to the telencephalon was recognized, and little was known about the other sensory systems as well. The work on sensory system organization in mammals allowed comparisons with contemporary and subsequent findings in nonmammalian vertebrates.

At the outset of this section, we need to note that the following paragraphs acknowledge only a small fraction of the people who have made seminal contributions to this field. It is in fact both awe-inspiring and daunting to survey one's collection of books and reprints and see name after name of other comparative neuroscientists and the copious amounts of material that they have published. Many laboratories and their members throughout the world—in countries including but certainly not limited to The Netherlands, Sweden, France, Spain, United Kingdom, Italy, Switzerland, Russia, Germany, Hungary, and Poland within Europe as well as Japan, Australia, New Zealand, Chile, Brazil, and other countries—have been omitted here. We can provide only a small sample, a brief glimpse into the foundations of the current views on forebrain evolution, and have thus tried to select at least representative contributions to this large arena. We recommend that the reader explore the three-volume, encyclopedic masterwork of Rudolf Nieuwenhuys, Hans ten Donkelaar, and Charles Nicholson, published in 1998, as well as the lists of references provided throughout this book for a broader appreciation of the field as a whole and its legion contributors.

Diamond, Kaas, Allman, and Krubitzer. The organization of the multiple ascending sensory pathways in mammals was first explored by Irving Diamond and his co-workers in the early 1970s at Duke University and has been studied extensively in the ensuing decades. This highly prolific and ground-breaking group also included John Harting, Vivien Casagrande, William Hall, John Jane, Herbert Killackey, and Bruce Masterton. In addition to an already known visual pathway from the retina directly through the dorsal thalamus to the primary visual neocortex, they found a second major visual pathway that proceeds from the retina first through the midbrain roof and then to the dorsal thalamus and thence to secondary, tertiary, and many further levels of visual cortical areas. Likewise, multiple pathways were identified for the somatosensory and auditory systems. All of these systems have multiple areas of neocortex that contain a full representation of the sensory world within them. More recently, Jon Kaas and John Allman proposed a theory of genetic replication to account for the evolution of these many sensory areas for each modality, areas that appear to have evolved independently to some extent in the various different mammalian radiations. Leah Krubitzer and her colleagues also have extended the studies of areal cortical specialization across mammals and proposed a theory of how duplication of cortical areas may occur.

Northcutt. In the late 1960s, R. Glenn Northcutt had independently questioned the traditionally accepted theories of telencephalic evolution. Over the subsequent several decades, he and his numerous students and other members of

his laboratory—of whom some of the earlier ones included Michael Pritz, Ann Butler, Andrew Bass, Mark Braford, Catherine McCormick, Mark Ronan, Walt Wilczynski, Timothy Neary, Georg Striedter, Shaun Collin, Helmut Wicht, and Mario Wullmann—extensively studied ascending sensory pathways in a wide variety of anamniote as well as amniote vertebrates. This work led to the finding that enlargement and elaboration of the brain, and specifically of the forebrain, have occurred multiple times independently within different lineages of vertebrates—not just in mammals as established by Diamond and his co-workers, but also in jawless vertebrates, cartilaginous fishes, ray-finned fishes, and in reptiles and birds—directly contradicting unilinear views of evolutionary change.

Northcutt presented an overview of this crucial insight in a 1981 paper, forming a foundation for his continued work. These findings and a host of additional experimental studies that have augmented and extended them have led to a new perspective in evolutionary neurobiology. Multiple instances of independent evolution of neural structures and connections in different radiations have been documented.

Scalia, Heimer, and Ebesson. A key series of experiments occurred during the same period of the late 1960s and early 1970s that addressed the question of olfactory domination of the telencephalon in ancestral vertebrates. Frank Scalia, Lennart Heimer, Sven Ebesson, and their co-workers found that olfactory projections in anamniotes are not widespread throughout the telencephalon. Rather, in contradiction to the traditional view, these projections were found to be limited to restricted areas in the lateral part of the pallium. Parenthetically, more recent work by Northcutt and his co-workers showing relatively extensive olfactory projections in hagfishes and lampreys has, however, reopened the question of the extent of olfactory projections in the earliest vertebrates. Although olfactory projections were indeed restricted in the ancestral stock of all jawed vertebrates, they may not have been so in the earliest jawless vertebrates.

Karten: Equivalent Cell Hypothesis

A series of experiments, carried out by Harvey Karten and his various co-workers, dramatically altered the traditional notions about the forebrain and its evolution. They led to the formulation of Karten's **equivalent cell hypothesis**, comparing various nuclear groups in the telencephalic pallium of birds with individual layers of the mammalian neocortex. This hypothesis was the inspiration and driving force for a major body of research on the neural organization of the brains of birds that produced seminal breakthroughs in many different areas from birdsong to basal ganglia organization to visual and auditory system organization and function to cognitive research. We will discuss the various theories of forebrain evolution in more depth in later chapters, particularly Chapters 19 and 25, but we will introduce the basic tenets of them here.

Harvey Karten, William Hodos, Walle Nauta, and their co-workers began their seminal studies at the Walter Reed Army Institute of Research in the early 1960s. Among other comparative neuroscientists there at the same or overlapping times were Sven Ebesson, Lennart Heimer, James Petras, Ford Ebner, Boyd Campbell, and William Mehler. The vision and support of

David Rioch and Joseph Brady allowed this highly talented group to flourish and subsequently found multiple radiations of comparative neuroscience research programs. Their work at the Walter Reed and subsequently at other institutions to which they variously moved laid the foundation for major discoveries about sensory system and forebrain organization in birds, which continue to influence the directions of research to the present day.

They found that, in birds, ascending sensory projections from the dorsal thalamus terminate in two regions within the pallium. One of these regions, called the Wulst, has layer-like organization, but the other region, called the dorsal ventricular ridge (DVR), is organized as a nucleus rather than as a cortex. Nonetheless, because of its connections and numerous other features subsequently found, the DVR is now widely recognized as a homologue of part of the mammalian pallium. A similarly organized DVR is also present in reptiles. Subsequent studies by a number of workers showed that it, like the DVR in birds, also receives several ascending sensory pathways, as does the dorsal, or general, cortex in these animals, a region homologous to the Wulst of birds. Thus, both birds and reptiles have similar sets of ascending sensory pathways via the dorsal thalamus to two different parts of the pallium, a layered or layer-like structure and the DVR. Since in mammals the dorsal thalamic projections to neocortex terminate predominantly in the fourth of its six layers, Karten proposed homology of the Wulst and DVR target zones of the thalamic afferent fibers to layer IV of neocortex.

The similar ascending pathways to the pallium in various reptiles were found first in turtles by William Hall and Ford Ebner and subsequently in crocodiles by Michael Pritz and in lizards by Laura Bruce and Ann Butler and also by Robert Foster and William Hall. Further, in 1971, Sven Ebbesson and Dolores Schroeder published findings of similarly organized ascending sensory projections to a nuclear area in the telencephalic pallium in sharks, suggesting that the organization of sensory systems and their afferent areas within the telencephalon might be similar in all vertebrates—mammals and nonmammals alike.

Karten's comparison of the thalamic afferent neuronal populations in the pallium of birds and reptiles to layer IV of neocortex (and of connected pallial regions in birds and reptiles to similarly connected other layers of neocortex) is called the **equivalent cell hypothesis**. He proposed that connective relationships between cell groups are specified by some factors specific to those cells, even if the cells are displaced or migrate in different ways during embryological development in the two different amniote radiations. Thus, cell populations present in various layers of neocortex would also be present in the Wulst and the dorsal ventricular ridge, located in various regions within these two structures and, for those in the DVR, having the form of nuclear groups rather than layers. The basic pattern of internal circuitry for neocortex is that layer IV projects to the more superficially lying layers II and III, which in turn project to the two layers deep to layer IV, layers V and VI. Likewise in birds, Karten compared the subsequent intrapallial connections for the sensory pathways with the cell populations of neocortical layers II and III and of layers V and VI.

Karten's equivalent cell hypothesis is currently a matter of some dispute. Other comparative neuroanatomists have recently challenged this notion, as discussed below. However,

as in many scientific controversies, where both sides have compelling evidence for their position, the truth often lies somewhere in between. While neither side has the whole picture, each is correct for the part of the picture that they do have. This would appear to be the case in the controversy over pallial evolution in the tetrapod line. Recent molecular evidence, from the work of Jennifer Dugas-Ford and Clifton Ragsdale, strongly supports a comparison of the DVR sensory-receptive nuclei and the similar portion of the Wulst with layer IV of the mammalian pallium and with other parts of the DVR likewise to layer V. The comparison of Wulst and DVR regions to layers of the mammalian pallium was Karten's crucial and most fundamental insight. It was revolutionary at the time and also was the key that changed the direction of research in this field and opened the door to a new level of interest in comparative neuroanatomy and comparative cognitive studies that has continued for over three decades.

Note that in the above paragraph, we used the phrase "layer IV of the mammalian pallium" rather than saying "layer IV of the mammalian neocortex." Therein lies the rub. Karten's equivalent cell hypothesis specified comparisons with the layers of neocortex. The dispute, summarized below, is whether the comparison should be with neocortex or with other parts of the pallium—specifically a pallial part of the amygdala and its associated structures. (As mentioned in Chapter 3, the amygdala is a collection of nuclei in the ventrolateral pallial region of mammals. It is particularly associated with species-specific behaviors and emotional processing, including threat recognition.) The molecular markers that label the sensory-receptive cell groups within the DVR and Wulst also label not only layer IV of neocortex but additionally the lateral nucleus of the amygdala, which is part of the frontotemporal amygdala (see Chapter 19) and *also* receives ascending sensory projections from dorsal thalamic sensory relay nuclei. In fact, this lateral amygdalar nucleus may simply be an elaboration of the same cell population that forms layer IV in the neighboring neocortex. Thus, whereas Karten's fundamental insight stands, there remain major differences in viewpoint as to how pallial evolution occurred in amniotes that are yet to resolve.

Other Theories of Pallial Evolution

We will explore the current set of theories of pallial evolution in greater depth in Chapters 19 and 25. Here, we will just briefly note the various positions that either support the idea that the DVR is evolutionarily related to neocortex and/or the idea that it is related to the frontotemporal amygdala, an amygdalar division identified by Larry Swanson and Gorica Petrovich that includes the lateral amygdalar nucleus.

Reiner and Butler. In the 1990s, Anton Reiner and Ann Butler independently supported a DVR-neocortex homology. Reiner's support for the DVR-neocortex homology derived mainly from comparisons of pallial cellular constituents and topological relationships. He found that the histochemical profiles of the cells in mammalian neocortex were not all represented in the pallium of turtles or other reptiles. Whereas cells with characteristics similar to those in the deep, infragranular layers, layers V and VI, of neocortex can be identified in turtle

general cortex, cells with characteristics similar to those in the main sensory-recipient layer IV and those in the more superficial layers, layers II and III, are scarce to absent in turtle cortex. Layers IV to II-like neurons are likewise absent in the dorsal ventricular ridge. Reiner thus proposed a modification to Karten's equivalent cell hypothesis, positing that the reptilian DVR and dorsal cortex and the mammalian neocortex evolved along separate lines, nonetheless having shared a common origin from a pallial region in the ancestral amniote stock. Reiner later further developed this view, positing a "common origin of the temporal neocortex and DVR hypothesis" for DVR homology. In support of this hypothesis he noted the cellular continuity of the DVR cell plate with that of the general/dorsal cortex in reptiles and the strong similarities of both connections and topology of DVR sensory regions to those of the more lateral, or temporal, parts of neocortex. Reiner postulated that a "proto-DVR condition" was evinced by the common amniote ancestor, which gave rise to neocortex in mammals, with the addition of more cell types and the definitive layers IV-II, and to the full-blown dorsal ventricular ridge in reptiles and birds.

Butler proposed a **dual elaboration hypothesis**, which was based on a cladistic analysis of the dorsal thalamus and the pallium. She identified two divisions of the dorsal thalamus, called the **collothalamus** and **lemnothalamus**, based on differences in their patterns of connections, which are present across at least all jawed vertebrates. Likewise, within amniotes, she identified corresponding collopallial (lateral) and lemnopallial (medial) parts of the neocortex in mammals and of the telencephalic pallium in reptiles and birds to which each thalamic division projects, respectively. In reptiles and birds, the **lemnopallium** is the dorsal, or general cortex (called the Wulst in birds), and the **collopallium** is the dorsal ventricular ridge. Butler posited that each division, collo- and lemno-, could evolve separately, with the collothalamus and collopallium having initially predominated in the diapsid line to reptiles and birds and the lemnothalamus and lemnopallium having initially predominated in the synapsid line to mammals. Secondly, birds elaborated their lemnothalamus and lemnopallium, while some orders of mammals secondarily elaborated their collothalamus and collopallium. Recent molecular evidence of gene expression patterns supports the basic division of the dorsal thalamus into lemnothalamic and collothalamic moieties.

Bruce and Neary. In 1995, Laura Bruce and Timothy Neary put forth a provocative new hypothesis, postulating that the anterior part of the DVR is homologous to the basolateral amygdala (more recently designated the frontotemporal amygdala). Although the posterior part of the DVR had long been regarded as homologous to the mammalian amygdala, its anterior part, which receives the various afferent sensory pathways from the dorsal thalamus, had been regarded separately and as a homologue of mammalian neocortex at that time. The Bruce-Neary hypothesis was based on cytoarchitectural continuity and on a new view of the homologies of the dorsal thalamic sensory relay nuclei. The collothalamic nuclei project not only to the neocortex but also to the lateral nucleus of the amygdala (a component of the frontotemporal amygdala). Some of them project predominantly to the amygdala and supply only a minor projection to the lateral, or temporal parts of neocortex, and

some evince the opposite pattern. Bruce and Neary compared the collothalamic nuclei of reptiles and birds with those that project predominantly to the amygdala rather than with those that project predominantly to the lateral, or temporal, parts of neocortex. They thus inferred homology of the anterior DVR to the frontotemporal amygdala rather than to any part of neocortex. The debate that has continued over the past decade hinges to a significant degree on determining what the exact correspondences of the collothalamic nuclei are across amniotes, an issue that has not yet been resolved.

Smith-Fernandez and Puelles and Rubenstein. Over the past 10 years, support for the anterior DVR-frontotemporal amygdala hypothesis has grown, although it is far from universally accepted. Anibal Smith-Fernandez and also Luis Puelles and John Rubenstein, each with their respective co-workers, independently identified a region in the ventrolateral part of the developing telencephalic pallium that is negative for certain regulatory genes, in contrast to the rest of the pallium. The model of pallial evolution based on these and related findings posits that the greater part of the pallial mantle differentiates into medial, dorsal (neocortical), and lateral pallial areas, while the ventrolateral-most pallial portion gives rise to what Puelles, Rubenstein, and their co-workers have designated as the ventral pallium. In mammals, the latter gives rise to several ventrolaterally lying structures, one of which is the lateral amygdalar nucleus. In reptiles, the ventral pallium gives rise to the major, sensory-recipient part of the dorsal ventricular ridge. This hypothesis thus needs to account for the origin of the lateral, temporal parts of neocortex, which also receive collothalamic inputs. It does so by positing that they evolved out of what was originally an exclusively lemnothalamic-recipient dorsal pallium, possibly by invasion by collateral axonal branches from the collothalamic-lateral amygdalar projecting neurons.

Martínez-García. Fernando Martínez-García and his co-workers, including Alino Martínez-Marcos and Enrique Lanuza, partially agree with the DVR-frontotemporal amygdala hypothesis, although they posit that the sensory-recipient homologue of the mammalian basolateral, or frontotemporal amygdalar division, is located in the more posterior part of the DVR. They view the more anterior part of the DVR as an independently evolved structure in reptiles and birds with no discrete homologue in mammals.

Butler and Molnár. Yet another and more recent perspective is that of Ann Butler and Zoltán Molnár, which is based partly on shared patterns of connections of the frontotemporal amygdala, particularly its sensory-recipient lateral nucleus, and the lateral, or temporal, parts of neocortex and partly on developmental considerations in the particularly crucial, ventrolateral part of the pallium. They proposed a field homology (see Chapter 1) of the anterior dorsal ventricular ridge to both the lateral part of the neocortex and the frontotemporal amygdala (and its associated structures) in mammals. They noted that a duplication of the embryonic territory that gives rise to the dorsal ventricular ridge in reptiles and birds might allow the production of two territories in mammals—the frontotemporal amygdala and its associated structures (claustramygdalar

formation) on one hand and the lateral parts of neocortex on the other. The similarities in afferent connections from the collothalamus, including the shared histochemical profiles of these sets of fibers, as well as similarities in efferent connections, could be explained as arising from a duplication event that would have occurred at the origin of the synapsid line to mammals.

Resolution of these various hypotheses on amniote pallial evolution will require additional research and the reconciliation of data on the patterns of connections with data on developmental gene expression patterns and other findings. It is perhaps not surprising that the evolution of the arguably most important part of the brain in mammals, the neocortex—at least the part that does uniquely distinguish mammals from other vertebrate taxa—is so difficult to illuminate. The degree of evolutionary divergence and elaboration is very high in this region across vertebrate taxa and, while rivaled in a few cases, is arguably not exceeded elsewhere in neural system evolution.

PERSPECTIVE

Continuing advances in cellular and developmental studies relevant to evolutionary neurobiology bode well for the future of this field. The methods of cladistic analysis, long recognized as valid and useful by zoologists, are also being applied to comparative neurobiology, and new insights into the relationship of ontogeny and phylogeny have clarified this long debated and confusing subject and provide a new and fruitful approach to the data. As discussed in Chapter 1, cladistics is an objective method, based on the distribution of a character, for inferring which characters in the brains of a group of species are ancestral (plesiomorphic) and which are specialized (apomorphic) in each particular species. As this methodology is applied more widely in comparative neurobiology, the evolutionary history of many parts of the nervous system within each of the major vertebrate radiations will be better understood. The method also can be applied to developmental stages and specifically to morphogenetic fields, as well as to structures in the adult phenotype, which will be of considerable advantage in illuminating the interactions of development and evolution.

Although ontogeny does not recapitulate phylogeny in the previously understood sense, it does recapitulate the features of an organism in terms of the organism's more general to more specific classification. As discussed in Chapter 3, four laws of development deduced by von Baer, a nineteenth-century German embryologist, can be applied to problems of nervous system evolution. These laws state that the more general features of an organism develop before the more specific features, so that, for example, a monkey embryo develops features common to all vertebrates before developing features specific to mammals and finally to monkeys. Thus, comparative studies of developing systems can reveal which features would have been common to the *developing* ancestors of a specified group.

These new insights allow for exciting new perspectives in comparative neurobiology. The work of Karten, Northcutt, Ebesson, and their co-workers was fundamental in establishing that differentiated, complex systems are widely distributed among vertebrates. A large body of recent work, including new

findings on the role of neural crest in head development, the recognition that enlargement and elaboration of neural structures have occurred independently multiple times within different vertebrate lineages, and other related new findings, allow for a reconstruction of many of the basic events that occurred in vertebrate brains over evolution. A recent application of cladistic methodology and the principles of von Baerian recapitulation to forebrain structures has also contributed to this reconstruction of evolutionary events, as have insights on developmental aspects of cellular organization in nervous systems, studies illuminating the role of homeobox genes during development in relation to the neuromeric organization of the brain, new perspectives on the evolution of specific cell populations as defined by their immunohistochemical profiles, and new perspectives on mammalian cortical organization and evolution. In the final chapter of this book (Chapter 31), we will be able to present a new overview of vertebrate brain evolution derived from these various lines of research.

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Part Two

THE SPINAL CORD AND HINDBRAIN

Overview of Spinal Cord and Hindbrain

OVERVIEW OF THE SPINAL CORD

The spinal cord, which is located within the backbone (**vertebral column**), is the portion of the central nervous system that makes contact with the body. The spinal cord is continuous with the caudal end of the brainstem. The spinal cord receives information from the external and internal environments of the body and executes commands to the organs of the body, both internal organs and external body parts. In addition, the spinal cord contains neural networks that integrate the incoming sensory information from various body regions and organize the specific commands to be given to the body parts. For example, a touch on one part of the body might, under one set of circumstances, provoke a movement of the animal to the right and, in another set of circumstances, a movement to the left. In addition to its own regulation of body function, the spinal cord supplies information about the body's internal and external environments to the brain and in turn is the route through which the brain controls the body. The integration of the actions of different body regions and communication with the brain are accomplished by long axons that run longitudinally within the cord.

Segmentation Within the Spinal Cord

During the embryonic development of the nervous system, the spinal cord develops in close accord with the vertebral column. Thus a pair of right and left spinal nerves exit between each pair of vertebrae, which are the individual bones of the vertebral column. The region of the cord from which one set of spinal nerves emerges is known as a **spinal**

segment. The term **spinal segmentation** is sometimes disconcerting to newcomers to spinal anatomy because they expect to see something like the segmentation of a worm and this is not the case; the surface of the spinal cord is smooth, with the exits of the spinal nerves giving the only clue to the location of the spinal segments. These segments, however, are not merely a device for teaching spinal anatomy; the spinal cord actually is organized according to segments as may be seen from the fact that spinal axons can be classified into two types: **intrasegmental** (those that remain within a segment) and **extrasegmental** (those that extend to one or more additional segments).

Each spinal segment is named for its corresponding vertebra. Thus, spinal segment L2 is so named because its nerve (spinal nerve L2) exits at the second lumbar vertebra. Likewise, spinal segment T6 is so named because of its association with spinal nerve T6 and the sixth thoracic vertebra. This is shown schematically in Figure 7-1, which shows several spinal segments and their corresponding vertebrae. For clarity, the spaces between the vertebrae have been exaggerated.

In most vertebrates, the spinal cord runs the entire length of the vertebral column. In some vertebrates, such as the anglerfish (*Lophius piscatorius*) and adult humans, the spinal cord ends well rostral to the caudal end of the vertebral column. This situation is due to differential growth in length of the vertebral column and spinal cord. Consequently, a given spinal segment may not be located within the vertebra of the same name, particularly for the more caudal segments. This, however, does not prevent the spinal nerves from exiting between the appropriate vertebrae, even though this point of exit is remote from the originating spinal segment. The result of this anatomical arrangement is that many spinal nerves must

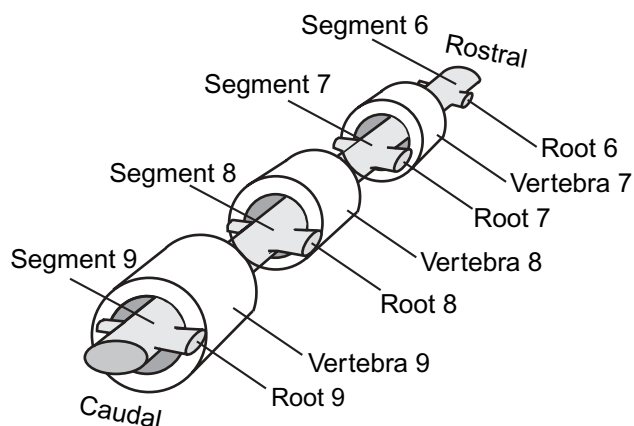


FIGURE 7-1. The relationship between segments of the spinal cord and their corresponding vertebrae. The spaces between the vertebrae have been exaggerated.

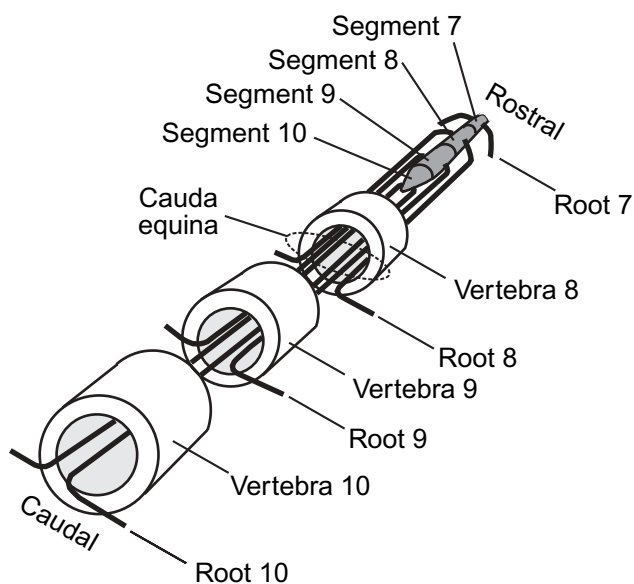


FIGURE 7-2. The cauda equina results from the shortening of the spinal cord so that it no longer entirely fills the length of the vertebral column. The spinal roots, however, continue to exit caudal to their corresponding vertebrae. For better visibility of the spinal cord, its surrounding vertebrae have been omitted.

pass well beyond the end of the cord before exiting. When early anatomists dissected the human spinal cord out of the vertebral column, they noted the resemblance of this collection of long spinal nerves that dangled well below the end of the spinal cord in the **vertebral canal** to the hairs of a horse's tail; they therefore named these nerves the **cauda equina**, which is horse's tail in Latin. Figure 7-2 shows the caudal end of the spinal cord. For clarity, the vertebrae that surround the cord have been omitted from the drawing. Only those vertebrae that exist caudal to the spinal cord are shown with the spinal nerves passing through them to form the cauda equina. Among non-tetrapods, the cauda equina is often (but not exclusively) found in fishes with a large head and a relatively small body.

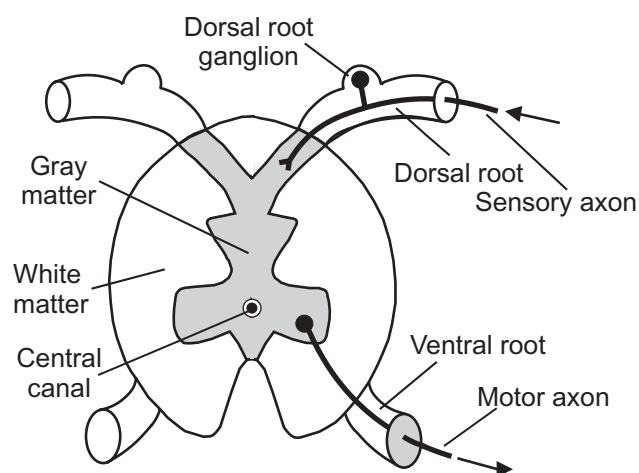


FIGURE 7-3. A transverse section of the spinal cord of a shark that illustrates the location of the dorsal and ventral roots, the dorsal root ganglion, sensory and motor axons, and the gray and white matter.

The segments of the spinal cord are named for their corresponding vertebrae of the vertebral column. These segments are grouped into regions according to the main body regions through which the vertebral column passes. The **cervical** vertebrae are the bones that support the neck. The **thoracic** vertebrae support the ribs that form the **thorax** (chest cavity). The **lumbar** vertebrae pass through the abdominal region; the **sacral** vertebrae are in the pelvic region; and the **coccygeal** vertebrae are in the tail. The spinal segment that sends its spinal nerve out at the fourth thoracic vertebra is thus the fourth thoracic segment or T4. Likewise, the segment that corresponds to the second lumbar vertebra is designated as L2 or the second lumbar segment. The numbers of vertebrae and their corresponding spinal segments vary according to the class of vertebrates; for example, virtually all mammals, irrespective of the lengths of their necks, have seven cervical vertebrae and eight cervical spinal segments—even giraffes.

Roots and Ganglia

Dorsal and Ventral Roots. The spinal nerves pass from the spinal cord to the periphery of the body (the limbs and internal organs such as the gut, the heart, etc.). When early anatomists traced these nerves back to the spinal cord, they observed that as these nerves neared the cord they divided into two **roots**, one dorsal and one ventral, which connected them to the spinal cord, much as a tree's roots connect it to the earth. Later research revealed that as a general rule (with some exceptions) incoming sensory axons enter the spinal cord via the **dorsal root** and motor axons exit via the **ventral root**. Figure 7-3 is a transverse section through the spinal cord of a shark. A dorsal root with a single incoming sensory axon is shown at the top. Below, the axon of a motor neuron is seen exiting via a ventral root. For clarity, only one sensory axon and one motor axon are shown in the figure. The actual number of such axons, however, can be considerable.

In addition to the axons of motor neurons that control skeletal muscles, the ventral roots also contain two other types of axons: (1) axons of cells that regulate smooth muscles and glands via the autonomic system and (2) axons that terminate not on muscle fibers, but on the muscle spindles. These motor neurons are known as **gamma efferents**. Their function is to activate the muscle spindles that are nestled among the muscle fibers and that respond to the tension of the surrounding muscle fibers. The interplay between the receptors on the spindles and their state of contraction as regulated by the gamma efferents results in smooth changes in tension and elongation of the surrounding muscle fibers.

In agnathans, the dorsal and ventral roots are not both present in the same spinal cord segment; the dorsal roots appear in one segment and the ventral roots in the next. In lampreys, the dorsal and ventral roots continue as separate nerves along their entire course. In hagfishes and other nontetrapods, however, the two roots come together to form a single spinal nerve, although the dorsal and ventral roots exit from the cord at somewhat different levels. In tetrapods, the dorsal and ventral roots exit at the same level of the spinal cord and, shortly after exiting, combine to form a common spinal nerve.

Ganglia. A prominent feature of the dorsal root is a swelling known as the **dorsal root ganglion**, so named because it appeared to the early anatomists to resemble a knot. The dorsal root ganglion contains the bipolar cell bodies of the sensory axons that are entering the spinal cord from somatic sources—the pain, touch, temperature, and stretch receptors of the skin, muscles, tendons, and joints—as well as from visceral sources—the internal organs of the body. Thus, for the spinal cord of jawed vertebrates, the afferent nerve components have been traditionally classified as **general somatic afferent (GSA)** and **general visceral afferent (GVA)**. In lampreys, an additional ganglion cell type is located within the white matter of the spinal cord. These cells are known as **dorsal cells** (originally called *Hinterzellen* and identified as ganglion cells by Sigmund Freud when he was still in medical school), and they convey information from mechanoreceptors for touch and pressure.

An additional ganglion occurs on the ventral root. This is known as the **sympathetic ganglion** and is an important part of the **sympathetic division of the autonomic nervous system**. The sympathetic division and its partner in the autonomic nervous system, the **parasympathetic division**, will be described in greater detail in Chapter 23. For now we simply will note that the cell bodies of these sympathetic axons are located within the gray matter of the spinal cord and that their axons leave via the ventral root. A short distance from the cord, these autonomic axons, known as the **preganglionic sympathetic axons**, leave the ventral root and enter the sympathetic ganglion. The preganglionic axons synapse on the cell bodies that are located within the ganglion. These cell bodies give rise to axons that leave the ganglion and rejoin the ventral root and are known as the **postganglionic sympathetic axons**. The postganglionic axons travel to the target organs of the autonomic system where they regulate the contraction of smooth muscles and the secretion of glands. A sympathetic ganglion and its pre- and postganglionic axons may be seen in Figure 7-7. Postganglionic axons travel to the various internal

organs of the body (collectively known as the viscera) and produce contractions of smooth muscles, such as those of the intestinal system, or stimulate glands to secrete.

The preganglionic neurons of the parasympathetic division are located in the brainstem and in the sacral region of the spinal cord. The axons of the parasympathetic neurons that are located in the brainstem also travel to the viscera and constitute the visceral components of the cranial nerves. The actions of the sympathetic and parasympathetic divisions of the autonomic system complement each other. In general, the parasympathetic division functions under normal circumstances and the sympathetic division takes charge of the viscera during situations that require short-term levels of high activity, such as during periods of emergency or stress. As you will see in our more detailed discussion of the autonomic nervous system, not all of the division of labor between the parasympathetic and sympathetic divisions, however, fits this generalization.

The preganglionic autonomic efferent fibers that exit in the ventral roots have traditionally been classified as **general visceral efferent (GVE)** components. Likewise, the motor axons that innervate the voluntary, somatic muscles of the body wall and the appendages traditionally have been classified as **general somatic efferent (GSE)** components. Like the preganglionic autonomic neurons, these motor neurons lie within the spinal cord gray matter rather than in peripherally located ganglia. As we will discuss later, the two general afferent components (GSA and GVA) and the two general efferent components (GVE and GSE) are all also present in the brainstem as components of various cranial nerves.

Columns of the Spinal Cord

We have used the term **vertebral column** rather than “spinal column” to refer to the column of bony rings that surrounds the spinal cord, so as to minimize confusion with the cell and axon columns that are internal to the spinal cord. The axon columns often are referred to as **funiculi** (singular = **funiculus**). The contemporary approach to the organization of the spinal cord is to consider the cell groups of the various segments also as forming longitudinal columns that are more or less continuous.

The cell columns consist of sensory-recipient and motor neurons (either visceral or somatic), cells of origin of **intra-segmental** axons, which remain within their own segment, and cells of origin of **extrasegmental** axons, which pass to neighboring segments, remote segments, or even may leave the spinal cord altogether to terminate within the brain. This latter type of extrasegmental axon is called **suprasegmental**. The axon columns contain:

- Axons of incoming sensory neurons, the cell bodies of which are located in the dorsal root.
- Extrasegmental axons originating in the spinal cord, but remaining within the spinal cord.
- Suprasegmental axons originating in the spinal cord, but ascending to the brain.
- Suprasegmental axons that originate in the brain and descend to the spinal cord or brain.

The axon columns of the spinal cord constitute the so-called **white matter** of the cord; the cell columns make up the so-called **gray matter**. The gray matter is concentrated around the central canal of the cord, which is the remnant of the lumen of the embryonic neural tube and which contains cerebrospinal fluid. The gray matter tends to extend out dorsally and ventrally; the dorsal extensions are known as **dorsal horns** (because of their appearance in a transverse section); the ventral extensions likewise are known as **ventral horns**. Occasionally, **lateral horns** are present as well. These horns are shown in Figure 7-4. In general, the ventral horns contain the cell bodies of somatic motor neurons, and the lateral horns contain the cell bodies of the preganglionic sympathetic neurons. The dorsal horns and the remainder of the gray matter contain the cell bodies of neurons that receive incoming

sensory axons or axons from elsewhere in the spinal cord. The dorsal half of the spinal cord gray matter—the dorsal horn—is embryologically derived from the alar plate, and the ventral half—the ventral horn and the preganglionic neurons of the autonomic nervous system in the lateral horn—is derived from the basal plate (see Chapter 3).

Another way of considering the columns of the cord derives from the results of experimental studies to trace the ascending and descending pathways in the spinal cord, particularly in tetrapods. These studies revealed that when the longitudinal cell columns are individually labeled, they take on the appearance of layers of **laminae** (singular = **lamina**). Figure 7-5 shows a hypothetical spinal cord with both axon and cell columns. For simplicity, only two axon columns and two cell columns are shown. The more medial of the two cell columns contains small cells and the more lateral contains larger cells. When a cross section of the cord is viewed, as in the shaded region at the left, the longitudinal organization of the columns of cell bodies cannot be easily recognized, but when appropriately labeled with a histochemical marker, the cells appear to be organized in a laminar arrangement. In other words, the “pie” is the same; it just has been sliced differently.

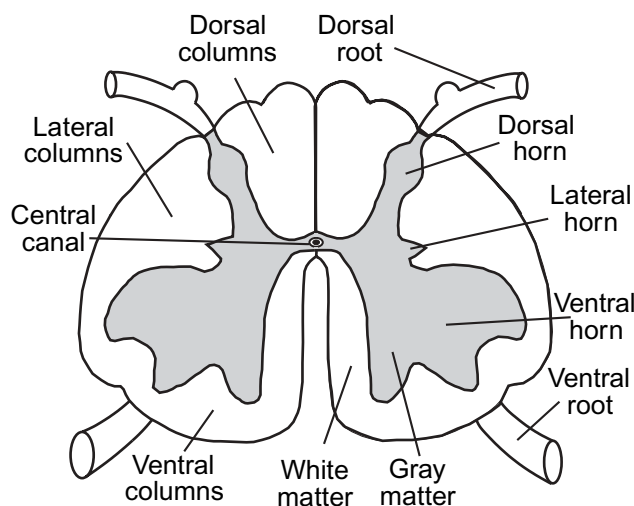


FIGURE 7-4. The white matter columns and the horns of the gray matter columns of a primate spinal cord.

Pathways Within the Spinal Cord

A number of axon pathways (also known as **tracts**) arise in the spinal cord and pass to the brain. Likewise, pathways originate in the brain and descend to the spinal cord. The pathways, like most of the pathways or tracts in the central nervous system, have two-part names, such as the tectospinal tract or spinocerebellar tract. The convention for naming pathways in the central nervous system is for the first part of the name to indicate the source of the pathway (i.e., the location of its cell bodies) and for the second part to reflect the target of the pathway (i.e., the location of its axon terminals). Thus, the tectospinal tract originates in the tectum and terminates in the spinal cord. Likewise the spinocerebellar tract arises from cell

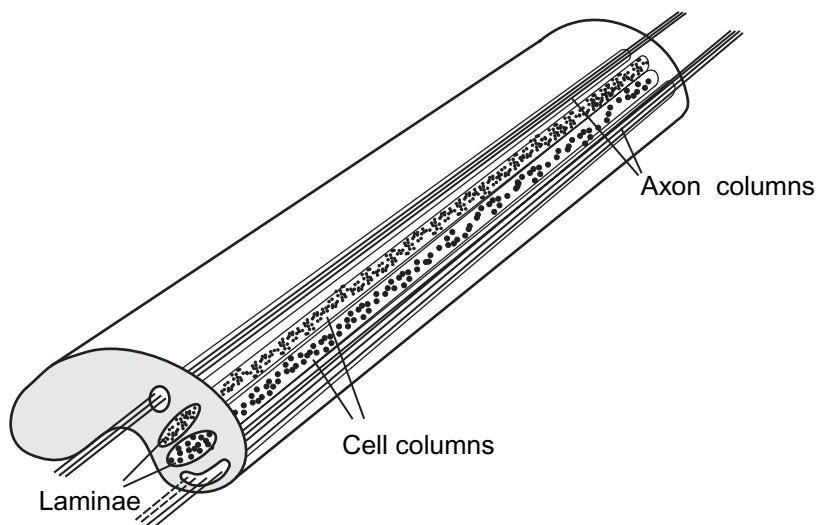


FIGURE 7-5. A hypothetical spinal cord showing axon and cell columns. When viewed in a transverse section (shaded region), the cell columns appear as laminae.

bodies located in the gray matter of the spinal cord, and its axons terminate in the cerebellum.

Apart from those spinal pathways that remain within the cord, the longitudinal axonal pathways may be classified into three types:

- Suprasegmental ascending pathways.
- Suprasegmental reticular pathways.
- Suprasegmental descending pathways.

Suprasegmental Ascending Pathways. These pathways comprise sets of axons that ascend from the spinal cord directly to their sites of termination in brain regions such as the cerebellum, tectum of the midbrain, and thalamus. These pathways are sometimes known as *lemniscal* pathways. The word *lemniscus* is a Greek word meaning band or ribbon and refers to such directly running pathways, in contrast to multisynaptic pathways like those that course through the more central parts of the brainstem, such as the reticular formation. Examples of ascending lemniscal pathways are the **spinocerebellar**, **spinotectal**, and **spinothalamic tracts**, which travel in the lateral and ventral axon columns of the white matter. Likewise, the **dorsal column system** is a lemniscal pathway.

The spinocerebellar tracts, which carry information about the state of contraction of the body's muscle groups and about the position of skeletal joints to the cerebellum, are present in all vertebrates. The spinotectal tract, carrying somatosensory information to the tectum of the midbrain, is present in sharks, salamanders, and amniotes (mammals, reptiles, and birds). Some evidence exists to suggest that this pathway evolved in ancestral vertebrates but subsequently was lost in ray-finned fishes and frogs. Spinothalamic tracts, which carry information about pain, temperature, and some forms of touch to the thalamus, have been described in lampreys and in some sharks but typically are found in amniotes. The dorsal column pathways contain the incoming axons of somatosensory neurons, the cell bodies of which are located in the dorsal root ganglia. These dorsal column axons terminate on two nuclei located in the caudal medulla close to its junction with the spinal cord—**nucleus gracilis** and **nucleus cuneatus**. The axons of these nuclei then ascend to higher levels of the brain via a tract called the **medial lemniscus**. Dorsal column pathways have been reported in agnathans as well as some other anamniotes, but are a consistent and prominent feature of tetrapod spinal cords.

Suprasegmental Reticular Pathways. Reticular pathways include both ascending and descending systems. The **spinoreticular tract** arises primarily from neurons in the spinal cord and terminates in the **reticular formation**, which, as will be discussed in detail in Chapter 13, is a collection of neuron groups that are located throughout the central nervous system from the spinal cord to the diencephalon. The spinoreticular tract appears to be common to all vertebrates and hence probably is a heritage from the earliest vertebrates. The principal cell groups that receive spinoreticular axons are located in the medulla, the pons, and the midbrain. The descending pathways of the reticular formation, mainly via the **reticulospinal tracts**, coordinate the activities of motor neuron populations that control specific muscle groups.

In nontetrapods, the other various descending pathways are very modest, but they are complemented by specialized, high-speed, giant-axon pathways from the reticular formation that provide for rapid control of movements by the brain. These giant axons, which are relatively few in number compared with the multitude of axons present in typical descending pathways, are not present in sharks and lungfishes.

Suprasegmental Descending Pathways. In tetrapods, particularly in amniotes, the descending pathways from the brain to the spinal cord are well developed. In addition to the reticular formation, descending pathways arise from multiple sites, including the midbrain tectum, vestibular system, midbrain tegmentum (red nucleus), and, in mammals, directly from the telencephalic cerebrum. The **tectospinal tract** carries motor commands from the midbrain tectum. The tectum contains “maps” of visual space, auditory space, somatosensory space, and, in those animals with electroreception, the electrical fields surrounding the animal. The **vestibulospinal tract** originates in the cell groups that receive sensory input from the vestibular organs. These organs, located in the inner ear, provide the animal with information about gravity and acceleration. Another movement-command pathway is the **rubrospinal tract**, which permits the cerebellum and some motor regions of the telencephalon to influence spinal motor neurons. In mammals and birds, direct pathways from the cerebrum to the spinal cord end on intermediary neurons as well as on motor neurons. In mammals, these axons are collectively called the **corticospinal tract**. Note that the vestibulospinal and reticulospinal pathways predominantly project to neurons that innervate extensor muscles, whereas axons of the corticospinal (where present) and rubrospinal pathways terminate predominantly on neurons that innervate flexor muscles.

Reflexes

One of the primary functions of the spinal cord is the performance of reflexes. These spinal reflexes are important for providing an automatic reaction of muscles in response to a stimulus. Some of these stimuli are the result of stretching or contraction of muscles. Stimuli that are painful or unexpected result in the reflexive withdrawal of a limb or the entire body. Some reflexes are excitatory in that they result in the activation of a motor neuron that in turn causes a muscular contraction. Other reflexes, however, are inhibitory and, therefore, prevent the activation of the motor neuron. Inhibitory reflexes are crucial in order to produce a cooperative activity of muscles; for example, one would not get very far if the flexor and extensor muscles (those that cause limb or finger joints to bend or extend) both tried to contract at the same time. Inhibitory reflexes prevent these opposing sets of muscles from contracting at the same time. This is especially important in walking and running. Inhibitory reflexes, working in smooth synchrony with excitatory reflexes, produce this coordination. Other spinal reflexes are visceral; that is, rather than controlling skeletal muscles they involve the actions of the smooth muscles of internal organs as well as the action of glands, such as sweat glands.

The simplest skeletal muscle reflex is the **monosynaptic reflex**, in which an incoming sensory axon from a muscle

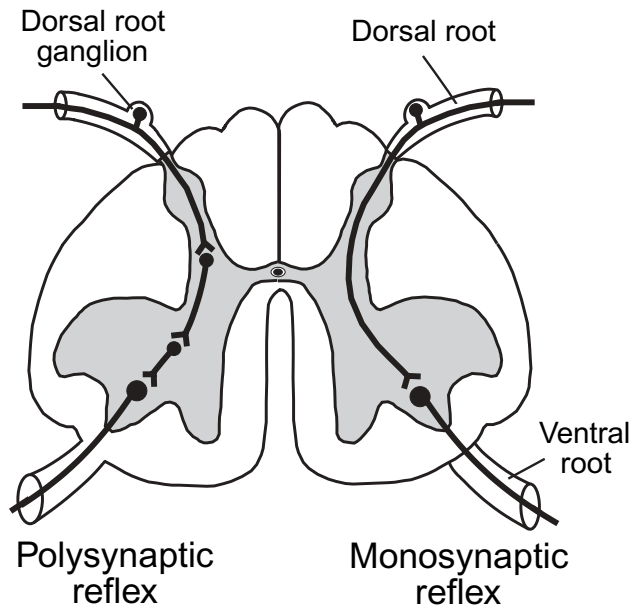


FIGURE 7-6. A transverse section through a primate spinal cord. The right side illustrates a monosynaptic reflex in which a sensory neuron enters via the dorsal root and passes directly to a motor neuron in the ventral horn. The left side illustrates a polysynaptic reflex in which two interneurons are interposed between the sensory and motor neurons.

receptor enters through the dorsal root and terminates directly on a motor neuron in the ventral horn of the gray matter. As shown in Figure 7-6, the motor neuron's axon passes out through the ventral root and terminates on a muscle near the original receptor. Since the only synapse in this circuit is that between the sensory axon and the motor neuron, this reflex is said to be monosynaptic. The patellar reflex, in which the lower leg jerks forward in response to a tap just below the knee cap, is an example of such a monosynaptic reflex. Monosynaptic reflexes are relatively rare, however. Most reflexes are polysynaptic and involve two, three, or more synapses between the incoming sensory axon and the motor neuron. Figure 7-6 also illustrates a polysynaptic reflex with two additional synapses between the sensory neuron and the motor neuron.

Figure 7-7 shows some of the pathways involved in a reflex of the sympathetic division of the autonomic nervous system. An incoming visceral afferent axon passes from the spinal nerve into the dorsal root and terminates in the gray matter on an intermediary neuron. This neuron, in turn, terminates on a preganglionic neuron located in the lateral horn of the gray matter. The axon of this preganglionic neuron leaves the spinal cord via the ventral root along with the somatic motor axons. Unlike the somatic motor axons, it does not leave the ventral root to enter the spinal nerve, but rather, almost immediately after leaving the spinal cord, it passes into the sympathetic ganglion where it terminates on the postganglionic, visceral motor neuron. The visceral efferent axon of the postganglionic

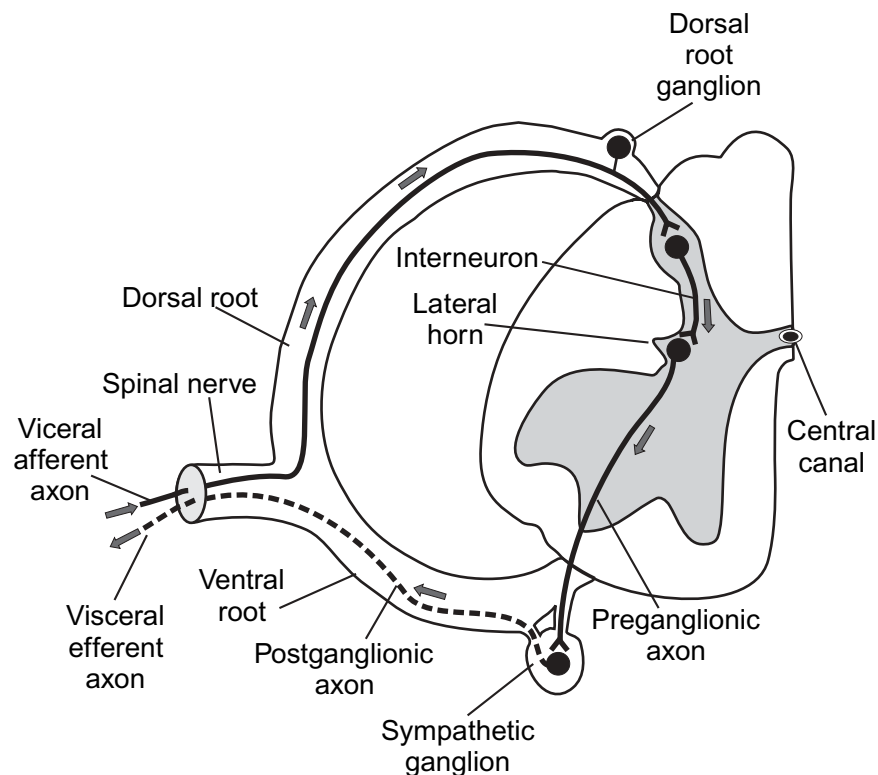


FIGURE 7-7. A sympathetic reflex arc. A visceral afferent axon terminates in the gray matter of the spinal cord on an interneuron. The interneuron sends its axon to a preganglionic sympathetic neuron in the lateral horn, the axon of which passes out to the sympathetic ganglion where it ends on a postganglionic sympathetic neuron. The postganglionic visceral efferent axon leaves the sympathetic ganglion and joins the axons in the ventral root as they enter the spinal nerve.

neuron leaves the sympathetic ganglion and joins the somatic efferent axons present in the ventral root as they leave the roots and enter the mixed, sensory and motor, spinal nerve. For clarity, the somatic afferent and efferent axons are not shown.

Spinal Autonomy

One indicator of the degree of the brain's control over the spinal cord is the extent to which the longitudinal axons increase in number towards the rostral end of the cord. In non-tetrapods, no substantial rostral increase in longitudinal axons is observed because most of the information remains within the cord. In contrast, in tetrapods, the existence of strong connections with the brain results in a build-up of longitudinal axons at the rostral end of the cord as each successive segment of the cord makes its axon contribution to the information flow to the brain and receives its axonal instructions from the brain.

The extent to which the spinal cord is an autonomous executive organ, more or less on a par with the brain, as opposed to being a subordinate that faithfully carries out the brain's instructions, depends on the type of environment that the animal inhabits and the evolutionary history of the species. In general, in nontetrapod vertebrates (agnathans, cartilaginous fishes, and ray-finned fishes), which inhabit an aquatic environment, the spinal cord has considerably more autonomous control over the musculoskeletal system than it does in tetrapods (amphibians and amniotes). In other words, the non-tetrapod spinal cord tends to carry out many of its postural and locomotor activities more or less independently of the brain. In particular, the spinal cord will coordinate its activities with the senses that are located in the head (vestibular, visual, lateral line, etc.) by way of such brain structures as the tectum, the cerebellum, and the reticular formation, all of which will be discussed in subsequent chapters. On the other hand, in some situations, such as threat from a predator, a brain region, such as the midbrain tectum, may execute temporary, high priority commands to the spinal cord and take complete charge of the body's movements during the duration of the emergency situation. In contrast, the tetrapod spinal cord generally is under the control of the brain more of the time; this is especially the case in mammals, which appear to have the highest degree of cerebral control of the body's posture and movements.

Rhythmic Movements and Central Pattern Generators

The neurons of the spinal cord form complex networks within an individual segment to coordinate the action of the muscles that are controlled by that segment. This is accomplished by networks of excitatory and inhibitory neurons that are symmetrical with respect to the right and left sides of the body. Intermediary neurons also coordinate the actions of large numbers of spinal segments to produce the coordinated activity necessary for propulsion of the body. A neuronal network or circuit that coordinates and synchronizes the actions of motor neurons is known as a **central pattern generator**. Ample physiological evidence supports the existence of central, neuronal networks that excite and inhibit the neurons in one or more segments of the spinal cord to produce the synchronized, rhythmic patterns of motor neuron excitation and

inhibition that result in smooth propulsion through the water or to locomote across the land or fly through the air. In fishes, central pattern generators cause oscillatory movements of the fins for steering, hovering, backward movement, and so on. These pattern generators are capable of producing rhythmic locomotor movements of the body (and limbs where present), even when the spinal cord has been surgically isolated from the brain. Respiration, although it involves muscles of the thorax and the diaphragm, is an autonomic function and is controlled by a central pattern generator located in the brainstem. In addition to the rhythmic movements of limbs and/or body for locomotion, tetrapods have certain other rhythmic body movements that are programmed by central pattern generators. These include scratching and chewing. Scratching is performed by spinal motor neurons. Chewing, being a specialized function of the head, is carried out by motor neurons located in the brain.

Although the central pattern generators of the spinal cord can operate in isolation as revealed in studies of isolated spinal cords, especially in lampreys, the pattern generators also are subject to influence from suprasegmental neuronal networks known as **command generators**. These are located in the hindbrain and midbrain. An example of such a command generator is the **mesencephalic locomotor region**, which is capable of initiating and maintaining swimming. Similar mesencephalic locomotor command generators have been found in other vertebrate classes as well.

OVERVIEW OF THE HINDBRAIN

The hindbrain, or **rhombencephalon**, is one of the major constituents of the brain. It consists of the **medulla** and **pons**. Its distinguishing features include a large number of nerves, known as **cranial nerves**, and the **cerebellum**. The caudal end of the hindbrain is the transition zone between the spinal cord and the brain. The hindbrain is, for the most part, an extension of the spinal cord that has acquired certain specializations and elaborations. Like the spinal cord, it has the following:

- *Afferent nerve components.* These are the sensory cranial nerve components, and they comprise two basic types: somatic and visceral. These nerve components have cranial nerve ganglia that are similar to the dorsal root ganglia of the spinal cord. The visceral afferents arise from internal organs of the body, as well as from several sources within the head. Likewise, the somatic afferent cranial nerve components are essentially the same as the somatic afferent spinal nerve components, except that the somatic spinal nerve components serve the body and the somatic cranial nerve components serve the receptors of the head.
- *Sensory neuronal populations on which the afferent nerve components terminate.* These are the sensory nuclei of the cranial nerves, which are similar to (and sometimes a continuation of) the sensory neuronal columns or dorsal horns of the spinal cord. Like the dorsal horns, the sensory cranial nerve nuclei receive input from both somatic afferent components that innervate the skeletal muscles and joints and visceral afferent compo-

nents that innervate the internal organs of the body. In general, however, the sensory nuclei of the hindbrain cranial nerves are specialized for head senses, such as hearing, taste, infrared detection, vestibular sense, lateral line mechanical sense, and electroreception, as well as pain, touch, and temperature sensations of the head, face, and oral cavity. The sensory neuronal populations of both the spinal cord and brainstem on which the incoming, bipolar, sensory neurons terminate are the first of a series of multipolar neurons in each sensory pathway. Thus, they can be referred to as **first-order multipolar neurons** (see Chapter 3).

- *Efferent nerve components.* These are the motor cranial nerve components. The somatic efferent neurons, like their spinal counterparts, terminate on the voluntary, striated muscles of the skeleton, but in the case of the cranial nerves, the muscles of the skeleton that they innervate are associated with the head, neck, and jaws. Additionally, somatic efferent neurons also innervate the muscles of the tongue and the extraocular muscles of the eye. Also as in the spinal cord, visceral efferent neurons constitute part of the autonomic nervous system. In the hindbrain, these neurons are parasympathetic. They do not terminate directly on the target visceral organs but instead are preganglionic; that is, they terminate on neurons in an external ganglion. The axons of these ganglionic neurons (the postganglionic axons) are the ones that directly innervate the viscera. Unlike the sympathetic ganglia (along the thoracic and lumbar parts of the spinal cord), the parasympathetic ganglia are located close to their target organs. Further details on the similarities and differences between the sympathetic and parasympathetic ganglia may be found in Chapter 23. Although most of the visceral efferent axons of the cranial nerves remain in the head, one nerve, the **vagus nerve**, follows a meandering course throughout the body as it innervates the internal organs of the thorax and abdomen.
- *Integrating and coordinating systems.* The spinal cord contains populations of neurons that are neither exclusively sensory nor exclusively motor. These coordinate the movements of muscle groups and provide central pattern generators for the production of rhythmic movements, such as walking, flight, and swimming. The hindbrain also has such integrating and coordinating systems, but they are far more elaborate than those of the spinal cord. The major integrating and coordinating systems of the hindbrain are the reticular formation and the cerebellum.

In brief, the reticular formation coordinates the activities of related groups of motor nuclei in the hindbrain and midbrain so that they act together and are not at cross purposes. In many vertebrates, the efferent axons of the reticular formation that descend to the spinal cord are the principal pathway for the voluntary control of body movement by the brain. Likewise, within the brainstem, other components of the reticular formation are involved in attention and wakefulness. Still others are the source of neuroactive substances that are transported to the forebrain.

The reticular formation consists of a large number of neuronal groups arranged in longitudinal columns of neurons (see Fig. 7-8). The most medial column is known as the **raphe nuclei**. The nuclei of the reticular formation are important sources of neuroactive substances that are transported elsewhere in the brain.

The cerebellum integrates sensory inputs from the somatosensory systems of the spinal cord and head, the vestibular system, and other sensory systems of the head with the outflow from various components of the motor systems of the forebrain. The cerebellum has been implicated in a large number of sensory and motor functions, especially balance, coordination, and smoothing of motor activity. Injury to the cerebellum can result in a loss of the smoothness of voluntary movements. The cerebellum, like the reticular formation, is a very complex division of the brain with multiple functions. For example, in those fishes that make extensive use of electroreception, the cerebellum is highly developed and plays an important role in the processing of this sensory information.

- *Axons of passage.* In addition to being the home of many specialized neuronal populations, the hindbrain is a major crossroad for axon systems ascending from the spinal cord to hindbrain, midbrain, and diencephalic sensory nuclei, as well as descending axon systems that originate in the telencephalon, diencephalon, mesencephalon, and hindbrain. These descending axon systems provide input to somatic motor neuron groups, preganglionic autonomic neurons, and integrating and coordinating systems in the hindbrain and spinal cord.

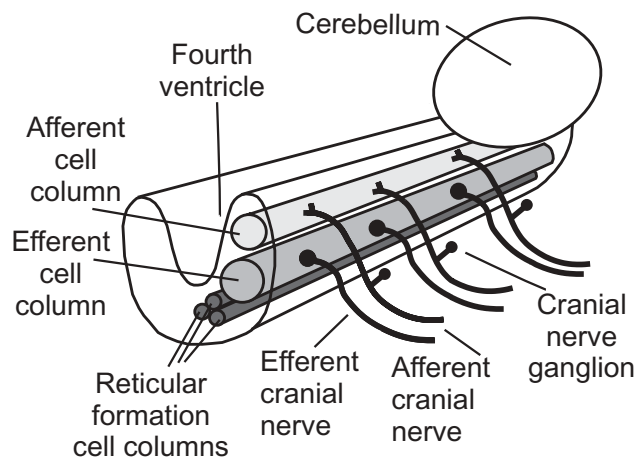


FIGURE 7-8. A schematic representation of the hindbrain. Caudal is to the left and rostral is to the right. Three cranial nerves, each represented by an afferent neuron and an efferent neuron, are shown. The afferent neuron, which could be somatic or visceral, is shown with its soma in a sensory ganglion and terminating in the afferent cell column, which corresponds to the dorsal horn of the spinal cord. The efferent neuron, which is shown with its soma in the efferent cell column, could be a somatic efferent axon or a preganglionic visceral efferent axon. Also shown in the figure are two integrating and coordinating systems of the hindbrain: the reticular formation, which is organized in longitudinal columns that run parallel to the afferent and efferent columns, and the cerebellum, which is located at the rostral end of the hindbrain.

The Obex and the Fourth Ventricle

A major feature of the hindbrain is the fourth ventricle. This is the most caudal of the four great brain ventricles and is located in the medulla. The fourth ventricle is fully or partially covered by the cerebellum depending on the cerebellum's size and shape. The caudal end of the ventricle forms a small fold of tissue known as the **obex** (Latin for bolt or barrier). The obex marks the location of the dorsal column nuclei, nucleus gracilis and nucleus cuneatus, which, as noted above, are important structures in the ascending somatosensory pathways from the spinal cord.

The Pontine Nuclei

In mammals, the hindbrain contains a prominent bulge on its ventral surface in the region of the pons. Part of this bulge is caused by the large number of descending axons that pass through the ventral hindbrain in this region. These descending axons are the corticospinal tracts and corticopontine tracts, which originate in the cerebral cortex and terminate in the spinal cord and pons, respectively. Intermingled among these axon bundles are the **pontine nuclei**. These nuclei receive the neocortical input and give rise to many axons that cross the midline to enter the contralateral cerebellum. These transverse axons that bridge the midline give the pons its name, which is the Latin word for "bridge." Birds also have pontine relays to the cerebellum, but their pontine nuclei are substantially smaller than in mammals. In reptiles and anamniotes, the pontine nuclei are small to absent.

Ganglia of the Cranial Nerves

The sensory neurons of most cranial nerve components, like their spinal cord counterparts, have their cell bodies located in ganglia on the roots of the nerves. Each ganglion has a unique name. Some of the names are descriptive, such as *semilunar* (half moon) or *spiral*. Sometimes they are named for their discoverer, such as the *ganglion of Scarpa* or the *Gasserian ganglion*. Sometimes the ganglia are named for their cranial nerve, such as *trigeminal ganglion*. Finally, the same cranial nerve ganglion can have all three types of names, which are used interchangeably; thus, the ganglion of the trigeminal nerve is also known as the semilunar ganglion and the Gasserian ganglion. The more frequently used names for the cranial nerve ganglia are given for reference in table format in Chapter 11. Those of you who will have occasion to do intensive reading in the literature of a particular cranial nerve will soon become familiar with the interchangeable names of its ganglion.

Organization of the Cranial Nerves

Figure 7-8 presents a highly schematic organizational plan of the hindbrain showing the organization of the major cell columns. Dorsally and laterally is the afferent cell column, which consists of the somatic sensory and visceral sensory cranial nerve nuclei. Ventrally and more laterally is the efferent cell column that contains the somatic motor neurons and the visceral preganglionic neurons. Medially and more ventrally are the cell columns that make up the reticular formation. At the

caudal end is the junction of the hindbrain and spinal cord. At the rostral end is the cerebellum and the junction of the hindbrain with the midbrain.

Embryology of the Hindbrain and a New Classification of Cranial Nerves

In Chapter 9, we will discuss the embryological development of the head, the brain, and the cranial nerves in considerable detail. Embryological studies are important because they offer many clues to the evolutionary history of the nervous system as well as the functional relatedness of components that might otherwise appear to be quite unrelated in the adult animal. Recent data on the embryological origins of the cranial nerves suggest a functional relationship between certain groups of cranial nerves that was not suspected previously. These new relationships have led us to propose a new classification of the cranial nerves based on their embryological origins and functional organization. Students often have difficulty understanding the cranial nerves because some have only afferent components, some have only efferent components, and some have both. Also the number of components in a given cranial nerve ranges from one to five. Further, a categorical distinction between "general" and "special" that traditionally has been made for some of the cranial nerve components is based on misconceptions about various aspects of embryological development. The new classification provides a framework for categorizing the various cranial nerve components according to their embryological origin and discards the erroneous assumptions of the traditional classification scheme.

Neural Tube, Neural Crest, and Placodes. As discussed in Chapter 3, the central nervous system develops from the **neural tube**, the rostral end of which eventually develops into the brain. Lateral to the neural tube is the **neural crest**, which is the embryological origin of a variety of tissues and contributes to the sensory and autonomic ganglia of the body as well as to the sensory and autonomic ganglia for a number of the cranial nerves. Another important embryological zone is unique to the head and is formed by the **neurogenic placodes**, which contribute to most of the sensory cranial nerve ganglia. Still a third group of cranial nerves—for light reception—develops from **evagination** of the forebrain. Except for the latter, the specific embryological origin (placodal and/or neural crest) of the neurons in each of the various sensory cranial nerves has yet to be fully established. Based on the present data, however, the cranial nerve components (mainly using mammals as the example here) can be categorized according to embryological origin as follows:

- *Sensory cranial nerve components that are derived from neural crest and/or neurogenic placodes.* These are the visceral and somatic afferent nerve components that innervate the internal organs of the body and the visceral and somatic parts of the head. Their afferent components convey information about 1) visceral sensations, 2) contact senses, such as touch, temperature, pressure, or pain, 3) the chemical senses of smell and taste, and 4) the distance and orientation senses that include hearing, lateral line senses (electroreception and/or mechanoreception),

and vestibular sense. Some of these nerve components have been traditionally classified as “general” and others as “special.” In some cases, their sensory bipolar neurons are derived mostly from placodes, in other cases mostly from neural crest, but in still another case the derivation is a mixture of both. Thus, derivation from neural crest versus neurogenic placodes does not provide a meaningful distinction for the general versus special designation. This issue will be covered in considerable depth in Chapters 9 and 10.

- *Sensory cranial nerve components derived from the neural tube.* These are for the light receptive senses and comprise the optic and epiphyseal cranial nerves. In actuality, these are tracts within the central nervous system rather than “nerves,” but they are listed with the true cranial nerves since they receive the light input and convey this distance sense information to other parts of the brain.
- *Motor cranial nerve components that are derived from the neural tube.* These are the motor neurons that lie within the basal plate-derived part of the brainstem. The visceral efferent neurons comprise the parasympathetic neurons of the head. The somatic efferent motor neurons innervate muscles of the eyes, jaws, face, throat, tongue, and neck and shoulder. As in the case of sensory cranial nerve components, the somatic motor neurons have traditionally been split into “general” and “special” categories, based on misconceptions of embryological development; this issue and its resolution will be considered in detail in Chapters 9 and 10.

Three particular cranial nerves of the hindbrain are often particularly troublesome for students because they seem to mix together unrelated functions. These nerves are the facial nerve, the glossopharyngeal nerve, and the vagus nerve. They all have multiple components (4, 5, and 5, respectively), and understanding them is best achieved by considering each component separately. In fact, as discussed in later chapters, we have separated each of these nerves into dorsal and ventrolateral divisions, which are consistent with their embryological origin and their functional attributes.

Efferent Axons in Afferent Nerves

Many, and perhaps all, of the sensory cranial nerves also contain efferent axons. These efferents are not motor but rather terminate on the receptors from which the afferent nerves receive their input. They appear to modulate the activity of the receptors and may play a role in attention.

EVOLUTIONARY PERSPECTIVES ON THE SPINAL CORD AND HINDBRAIN

The ancestors of land vertebrates were a group of fishes known as the **rhypidistians**. Rhypidistian fishes belong to the sarcopterygians, which are the fleshy-finned fishes, as distinguished from the overwhelming majority of fishes, the ray-finned fishes (actinopterygians). Among the modern

sarcopterygian fishes are the lungfishes, which have the type of fleshy fins from which limbs evolved. These fleshy fins are quite different from the ray fins of teleost fishes, which typically lack sufficient mechanical structure to support the weight of the animal in very shallow water or on land where the aquatic buoyancy of the animal is absent.

The Transition to Land

One of the most far-reaching events in the evolution of the vertebrates was their invasion of the land. The entry of vertebrates into a vast and varying environment permitted the development of a large number of highly diverse species with an incredible variety of new adaptations for survival. More than anywhere else in the central nervous system, this major evolutionary change and its subsequent refinements and modifications are reflected in the spinal cord and hindbrain. Indeed, since many of these adaptations involved behavior, they depended upon the central nervous system to supervise and perfect their execution. Many of the adaptations involved the head because feeding, hearing, and other behaviors are quite different in air and in water. These will be discussed in some detail in later chapters. For now, we will concern ourselves with the main adaptations of the body that are required for life outside of the water. These are the structures necessary to compensate for the body's loss of buoyancy when it leaves the water and executes a locomotor pattern across a solid surface.

Amphibians are animals that may be characterized by their partial transition to the land; i.e., they are not completely terrestrial vertebrates. They are a mixture of terrestrial and aquatic characteristics. Ancestral amphibians tended to confine their existence to coastal regions or nearby aquatic areas. Alfred S. Romer, one of the 20th century's foremost comparative anatomists and paleontologists, came to the conclusion that sea fishes became progressively adapted to the less saline waters of rivers and estuaries. As the invasion progressed farther upstream, some animals became trapped in ponds as flood waters receded. Those that were able to survive in the pond environment flourished there. One problem with ponds is that they often become dry. Those ancestral pond fishes that had stubby, fleshy fins, rather than the thin, delicate fins typical of most modern bony fishes, were able to use these stubby, fleshy fins to drag themselves across the land to a nearby pond that still had water. By so doing, they were able to survive and transmit this characteristic on to subsequent generations. Those that could not move across land remained trapped in their diminishing ponds. The fleshy fins of these successful pond dwellers became the limbs of their tetrapod descendants. A number of species alive today survive by routinely making the transition from the aquatic environment to the terrestrial environment as part of their normal mode of existence as a reaction to decreased oxygenation of the water or decreased food supply. Examples include the climbing perch (*Anabas testudineus*), which does not actually climb but does locomote across dry land quite well, and the walking catfish (*Clarias lazera*). Other reasons for the invasion of land include reduced competition for resources, increased opportunities for successful reproduction and development of the young, and avoidance of larger predators by seeking shallower water.

Figure 7-9 illustrates the evolution of the ancestral sarcopterygian pectoral fin and the actinopterygian pectoral fin from the pectoral fin of ancestral vertebrates. The tetrapod forelimb is a modification of the sarcopterygian pectoral fin. Early tetrapods did not have the five-digit limbs that characterize later tetrapods. Six or eight digits were common in these animals.

Initially, the limbs could only permit these early tetrapods to drag their bodies across the ground. As anyone who has ever done anything similar will recognize, such dragging could cause injuries to the skin and abdominal muscles of the animals. Thus, animals with somewhat longer fins, or limbs as we will now call them, would have a lower risk of injury, and hence a better chance of survival. Thus began a trend to support the body off the ground that ultimately led to such specializations as the hooved legs of horses and sheep, the wings

of birds and bats, the hands of raccoons and primates, the paws of tigers and wolves, and many other variations including the upright, bipedal posture of birds and humans.

The neural apparatus to operate these specialized limb structures in a coordinated, integrated way is present in the spinal cord and accounts for the differences between the non-tetrapod and tetrapod spinal cords. With the development of long axon descending pathways from the brain, spinal autonomy diminished considerably. Other specializations for terrestrial life occurred in the head and included the development of the tongue and salivary glands to compensate for the loss of the water column that carries food through the mouth towards the digestive tract in nontetrapods. Modifications to the jaws permitted the capture of prey on land and the grinding and shearing processes necessary for the conversion of plant material into a digestible form.

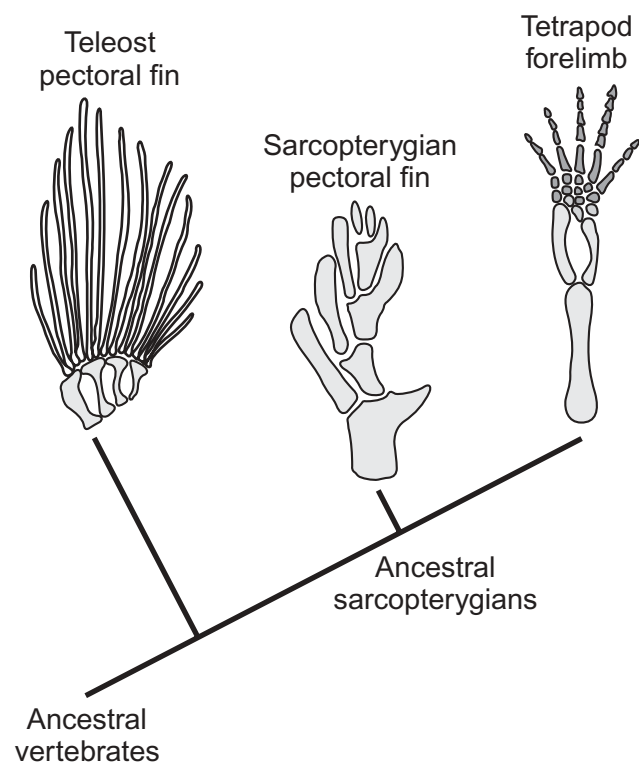


FIGURE 7-9. A cladogram showing the evolution of the tetrapod forelimb and the pectoral fin of teleosts from the pectoral fin of ancestral vertebrates. The fin of a perciform teleost is shown on the left; the sarcopterygian limb of *Eusthenopteron*, an extinct osteolepiform rhipidistian, is shown in the center; and the limb of an extant tetrapod is shown on the right. The bony elements in each forelimb are shaded in gray. None of the skeletal elements in the fins of teleost actinopterygians are homologous to any of the elements of the sarcopterygian and tetrapod limbs, since they develop from different parts of the fin/limb anlage. Both of these parts were present in ancestral vertebrates and are retained in elasmobranchs and basal bony fishes (bichirs and sturgeons). Most or all of the most distal parts of the tetrapod limb, the bones of the hands and feet, may have been uniquely evolved at the origin of this taxon, as indicated by their darker shading. Redrawn from Wagner and Chiu (2003) and used with permission of MIT Press.

Tetrapod Locomotor Patterns

The invasion of the land required a locomotor pattern quite different from that necessary for survival in an aquatic environment. Once out of the water, the body's buoyancy no longer counteracted the pull of gravity. On land, the tetrapod's limbs support its body's weight above the ground, and, in order to move forward, one or more limbs must be lifted off the ground. Once a limb is off the ground the body's weight must be carried by the remaining limbs. If the animal is to maintain its balance and not fall over, this weight must be so distributed that the center of gravity is now positioned appropriately over the limbs that remain on the ground. All of this shifting of weight must occur in synchrony with the raising and lowering of the limbs in order to result in a smooth forward progression across the ground. To complicate matters further, a pattern of raising and lowering of limbs that is suitable for one speed of locomotion is less suitable for another. Tetrapods have evolved several patterns of locomotor progression to deal with these problems.

The simplest locomotor pattern is walking, in which one leg is raised and moved forward at a time. When one leg is off the ground, the body's weight is shifted over the tripod formed by the three legs that remain on the ground. When that leg is back on the ground, a leg on the opposite end of the body is raised. For example, if the right foreleg is raised first, then the next leg to be raised is the left hind leg. Perhaps the best way for a biped like you to understand tetrapod locomotor progression is to temporarily return to tetrapod status by getting down on your hands and knees and crawling forward like a human baby would. Notice that if you allow your hands to support your weight as well as your knees, when you lift one hand to move it to a forward position, your weight is still nicely supported by the other hand and the knees, although you will have to lean a bit toward the hand on the ground to keep from falling over. If you now try to move the other hand forward, without shifting your weight to your knees, you will fall on your face. The only way you can move forward is by lifting one of your knees; the most comfortable one to lift will be the one that is on the side opposite to the hand that was just moved forward.

For faster forward progression, tetrapods use a pattern in which a front and back limb are off the ground at the same

time. When the two elevated limbs are on the opposite sides of the body (e.g., right forelimb and left hindlimb), this pattern is called trotting. When the two elevated limbs are on the same side of the body (such as right forelimb and right hindlimb), the pattern is called pacing. Readers who are familiar with horse racing will have come across these terms before. Finally there is running, which is actually a series of jumps in which the animal pushes off with its hind legs, passes through a brief period in which all four limbs are in the air, and then lands on its forelegs.

Birds, like humans and a few other mammals, are bipeds and, therefore, have different patterns for locomotor progression. Some birds walk like humans by lifting one of their two legs at a time while carrying the body's weight on the other. Others use a hopping progression, which is a series of short leaps in which both legs are in the air at the same time. The latter pattern of locomotion across the land also is used by kangaroos and anuran amphibians (frogs and toads).

Many tetrapods spend a portion of their time in the aquatic environment; examples of these are the majority of amphibians, some reptiles, a number of species of birds such as waterfowl, gulls and other shorebirds, and penguins as well as a number of mammals such as beavers, otters, seals, walrus, and some humans. Some mammals, particularly the whales and porpoises, are permanently aquatic. Many of these animals use the hindlimbs as the principal propulsion organs. These limbs often are used as paddles, alternating the right and left limbs. Frogs move forward through the water by forcing water from between their powerful hind legs by rapidly bringing them together. Those animals with powerful tails, such as alligators, propel themselves through the water by means of rhythmic side-to-side movements of their tails. Marine mammals use up-and-down rhythmic movements of the hindquarters of their bodies to move forward through the aquatic environment.

Another important mode of animal locomotion is flight. Birds and bats rhythmically move the large surface areas of their forelimbs to produce lift and forward movement through the air. Unlike some aquatic birds that paddle through the water with their hind limbs, penguins locomote through the water with their forelimbs the way that other birds locomote through the air; that is, they "fly" through the water.

Each of these specializations for the tetrapod life has its corresponding specializations in the sensory, motor, and intermediary neuron populations of the spinal cord and their continuations into the caudal hindbrain. Likewise these changes are reflected in various axon columns of the spinal cord and hindbrain. These changes will be discussed in detail in subsequent chapters.

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8

The Spinal Cord

THE SPINAL CORDS OF NONTETRAPODS

The principal form of locomotion of nontetrapods is based on rhythmic, undulatory movements of the trunk and tail muscles, often supplemented by movements of the fins. Much of the organization of their spinal cords is related to this locomotor pattern. In addition to normal locomotion to get from place to place, several sudden and very rapid forms of locomotion are required; these include rapid, evasive responses at the approach of a predator and sudden strikes to capture prey.

Muscles and Locomotion

The majority of nontetrapod animals locomote by means of rhythmic undulations of the body. The contractions of the corresponding muscles of the right and left sides must be coordinated to produce the smooth, rhythmic pattern of activity that propels the animal through the water. In those animals in which the fins assist in locomotion, the actions of the fins must be coordinated with each other and with the rhythmic movements of the body.

The muscles of nontetrapods differ from the familiar arrangement of muscles in tetrapods in which individual, specialized muscles are attached to the vertebrae, ribs, and limb bones. In contrast, the muscles of nontetrapods consist of segmented, sheet-like muscle masses known as **myomeres**. These myomeres are arranged as sequential, chevron-like segments along the body cavity. The organization of muscle fibers into myomeres rather than into discrete muscles has resulted in a

somewhat different organization and location of motor neurons within the spinal cord in nontetrapods.

Cell and Fiber Columns

Figure 8-1 illustrates the locations of a number of spinal cord cell and fiber columns in a transverse section through the spinal cord of a lamprey. The right half of the drawing shows the axonal columns of the cord, and the left side shows some of the principle cell types and the location of the giant axons that are a major feature of the non-tetrapod spinal cord. Of these, the **Müller axons** are situated in the ventral column, ventral to the dorsal horn of the gray matter, and the **Mauthner giant axon** is located in the lateral column, just lateral to the ventral horn of the gray matter.

Among the cell types that are present are the motor neurons of the ventral horn and the **dorsal cells** of the dorsal horn. Some of the dorsal cells receive input from mechanoreceptors of the skin and are specialized for the reception of touch, pressure, or pain. Some dorsal cells terminate on motor neurons that control fin muscles. Other axons of the dorsal cells enter the dorsal columns where they ascend to the hindbrain, the cerebellum, and other brainstem regions. Finally, some dorsal cell axons terminate on lateral neurons. These neurons both excite and inhibit motor neurons as well as other neurons. The lateral neurons have a large lateral dendrite that extends to the lateral edge of the cord. Other branches of their dendrites pass to the vicinity of the Müller axons.

The edge cells shown in the figure are a type of cell known as **marginal cells**. They are located outside the gray matter of the cord and probably are involved in the detection of the

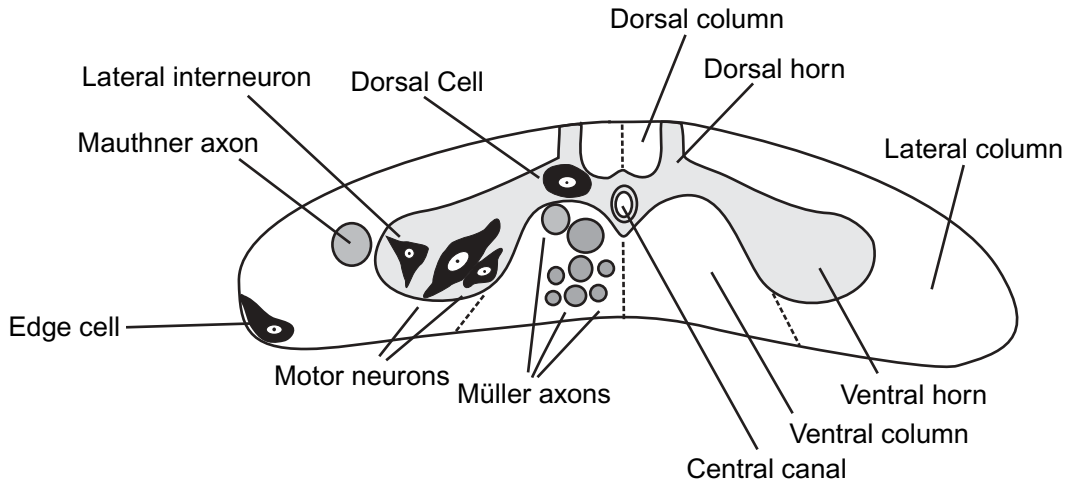


FIGURE 8-1. A transverse section through the spinal cord of a lamprey. The right side of the figure shows the locations of the gray matter horns and the axonal columns. The left side shows some of the major cell types and their locations as well as the locations of the giant Mauthner axon and giant Müller axons.

flexion of the spinal cord. Marginal cells will be discussed in greater detail later in this chapter.

Another type of cell, found in teleosts, are the **supra-medullary cells**. These are giant cells located at the dorsal surface of the spinal cord, above the gray matter. Because of their location in the cord, their similarity to spinal ganglion cells, and their axon in the dorsal root, supra-medullary cells had been regarded as sensory. A recent study, however, indicates that, in at least in one species of teleost (the puffer fish, *Takifugu nuphobles*), the supra-medullary cell axons terminate in cutaneous mucous glands, which suggests a motor rather than a sensory function. To complicate the picture further, some evidence indicates that peripheral processes of the supra-medullary cells also reach the epidermis. This raises the possibility that these cells may be both sensory and motor, in which case they would be providing changes in skin mucous in response to epidermal stimulation without benefit of an intervening synapse.

The cell bodies of some of the neurons with mostly local projections are located in the gray matter. Among these is a group of neurons known as the **commissural cells**, the dendrites of which spread in all directions; an example of one of the many types of commissural cells is shown in Figure 8-2. The commissural cell axons cross the midline of the cord to the opposite side and then either ascend, descend, or form a T-shaped bifurcation, with one branch of the axon running in the rostral direction and the other running caudally to one or more segments in each direction. This system of commissural neurons is primarily an intrinsic spinal system that coordinates the actions of various intermediary neurons and motor neurons in one or more segments of the cord. Some commissural cell axons, however, do ascend to the brain. Commissural neurons play an essential role in the generation and maintenance of swimming rhythms in nontetrapods.

The motor neurons of the nontetrapod cord form a relatively uniform column in the ventral horn of the gray matter.

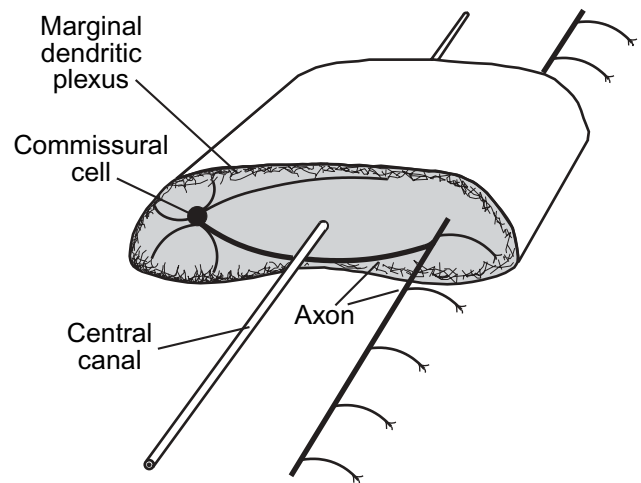


FIGURE 8-2. A commissural cell that sends its dendrites into many areas of the spinal cord, including a branch that passes over the central canal to the contralateral side. The cell's axon passes under the central canal to the contralateral side where it bifurcates into two long branches, one ascending and one descending. Each branch gives off many collaterals along its path.

In contrast, in tetrapods, the motor neurons of the ventral horn, while still forming a column, tend to be grouped into clusters of neurons that are sometimes known as "motor neuron pools" that correspond to specific muscles. Some motor neuron pools exist in the nontetrapod cord as well: that is, those that control the muscles of moveable fins, such as the pectoral fins, which are used in locomotion and also in hovering in one location. Groups of motor neurons that innervate specific muscles of the pectoral fins are located at the rostral end of the spinal cord in the ventral horn. Another example of

motor neuron pools in nontetrapods is the motor neurons that control the generation of sounds in certain groups of fishes (see Chapter 12). These sounds, which play a role in courtship behavior, are generated by the drumming of specialized muscles on the walls of the swim bladder, which is a taut bladder filled with respiratory gases that these fishes otherwise use for regulating their buoyancy in the water. This motor neuron pool is located at the junction of the rostral end of the spinal cord near its junction with the medulla.

Figure 8-3 illustrates a lamprey motor neuron with a dendritic tree that extends into the marginal dendritic plexus and an axon that leaves the soma and extends toward the periphery. Two types of motor neurons have been distinguished in the ventral horns of the nontetrapod spinal cord. The **primary motor neurons** are large and are relatively few. The **secondary motor neurons** are smaller in size and are more numerous. These two motor neuron types correspond roughly to two types of muscle fibers: the white fibers, which are fast in their contractions, and the red fibers, which are slower. Thus, in nontetrapods, the white muscles are used for fast swimming, such as pursuit of prey and escape, whereas the slower, red muscles are used for more leisurely swimming. In general, the primary motor neurons innervate the faster, white muscle fibers, and the secondary motor neurons innervate the slower, red muscle fibers, although in some nontetrapods, the secondary motor neurons also innervate some white fibers. The specific activities of these motor neurons are coordinated by the interneuron circuits known as central pattern generators.

Giant Axons and Escape

In addition to normal locomotion, escape from danger is an important function of the motor system. The detection of a potential threat, usually by the brain, breaks the normal locomotor pattern and results in a sudden, rapid change in direction and speed that is known as the *escape pattern*. To be effective, an escape pattern must be as rapid as possible since every wasted millisecond increases the likelihood of being someone's dinner. Since the velocity of a nerve impulse increases with the diameter of the axon, escape systems tend

to be associated with axons of impressive diameter, which is to be expected since those fishes with smaller diameter axons in their escape systems are less likely to escape than those with the larger diameter axons. Two types of giant axons have been described in nontetrapods: the **Müller** and the **Mauthner axons**.

Müller Axons. The Müller axons are found in agnathans and at least some teleost fishes. They originate from a small number of neurons with very large somata that are located in the midbrain and in the medulla. The majority of these axons cross the midline and descend in the white matter of the spinal cord to the caudal region of the cord where they synapse on motor neurons. They control both normal swimming and escape and vestibular control of orientation of the body to acceleration and gravity.

Mauthner Axons. In agnathans, teleost fishes, and many amphibians, the escape response is orchestrated by one of the most remarkable neurons to be found in any central nervous system: the Mauthner cell. And when we say "one," we mean precisely that; only one Mauthner cell exists on the right side of the nervous system and only one on the left. The Mauthner cell, which consists of a giant cell body located in the medulla, in the vicinity of the termination of the vestibular branch of nerve VIII, has been most thoroughly studied in teleost fishes and agnathans. These cells often are absent in bottom-dwelling species that do not move very much. An illustration of a Mauthner cell can be seen in Figure 8-4.

The Mauthner cell body consists of a banana shaped soma with two enormous main dendrites, one pointing ventrally and one pointing laterally. The Mauthner soma often has a diameter as great as 0.10 mm and a total length of nearly 1.0 mm in goldfish. The main dendrites can extend as far as the outer margins of the brainstem. Each Mauthner cell can have tens of thousands of synaptic terminals on it. Smaller dendrites also are present on the soma, but they are not as spectacular as the two main dendrites. The total number of synaptic terminals can be several hundred thousand. Although most of these terminations

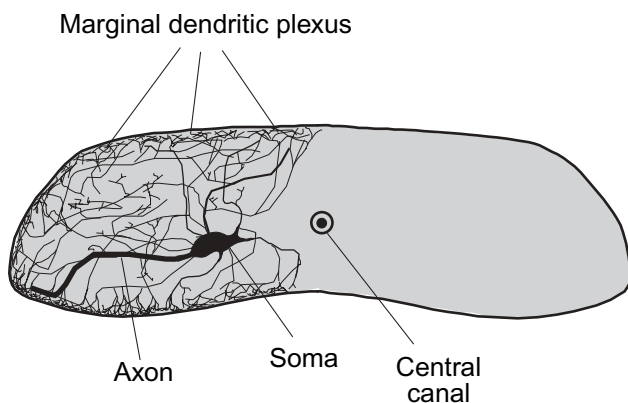


FIGURE 8-3. A lamprey motor neuron with numerous dendritic branches that spread out across the white matter of the cord and an axon that is leaving the spinal cord en route to myomeres of the body.

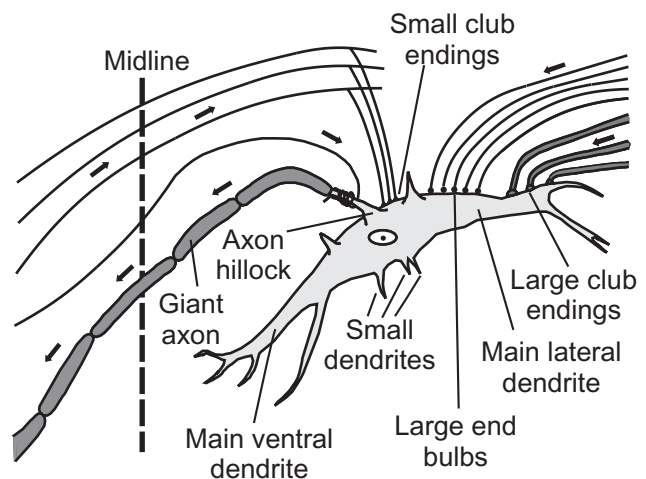


FIGURE 8-4. The giant Mauthner cell, which has a giant, heavily myelinated axon that crosses the midline and descends to the spinal cord on the contralateral side.

BOX 8-I. Neuroactive Substances in the Spinal Cord

The spinal cord is the caudal extension of the hindbrain that controls the musculoskeletal and autonomic functions of the body. Like the brain, it is the origin and termination of many peripheral nerves, some of which are sensory and others of which are motor. In addition, like the brain, it contains local neuronal populations that perform various integrative functions. It is, therefore, not surprising that many of the same neurochemical mechanisms that occur in the hindbrain and at higher levels of the central nervous system also are found in the spinal cord.

Some neuroactive substances are found predominantly (although not exclusively) in the spinal cord, such as glycine, substance P and L-enkephalin. Others are found widely distributed in both the brain and spinal cord, such as dopamine, serotonin, glutamate, and GABA. Among the most common spinal cord neuroactive substances are:

- Acetylcholine
- Glutamate
- GABA
- Glycine
- Serotonin
- Dopamine
- Norepinephrine
- Vasoactive intestinal polypeptide (VIP)
- Neuropeptide Y (NPY)
- Substance P
- Leucine enkephalin
- Calcitonin gene-related peptide (CGRP)
- Nitric oxide

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are chemical synaptic junctions, a considerable number of junctions are electrical or mixed chemical/electrical, which result in a faster speed of transmission. Many of the axodendritic synaptic terminals form an unusual type of structure known as a “club ending” because of their shape. Other terminations on

the Mauthner nerve are spiral in shape. These are axoaxonic and are wrapped around the axon hillock where the giant axon emerges. The spiral terminations are inhibitory and are ideally situated to suppress an action potential from being propagated down the giant axon.

The inputs to the Mauthner cell are mainly from the vestibular, auditory, and lateral line systems. The latter system contains two types of receptors: (1) mechanoreceptors that respond to such stimuli as vibrations, pressure waves, and water flow across the surface of the head and body, which are important in detection of predators, maintenance of schooling, and other behaviors; and (2) electroreceptors that indicate features of electrical fields in the surrounding water. These auditory, vestibular, and lateral line axons terminate mainly on the main lateral dendrite. Other sources of stimulation from the tectum, the cerebellum, and the visual system have also been described.

Shortly after its emergence from the axon hillock, the giant Mauthner axon sends a small collateral branch back toward the axon hillock. This **recurrent** (flowing back) branch terminates on a small, inhibitory interneuron, which in turn terminates on the axon hillock. This **recurrent inhibition** results in discrete pulses of muscle stimulation. Such a mechanism is known in engineering as “negative feedback”; it is essentially the same as the mechanism by which a thermostat shuts off the furnace when the room gets warmer than its set point.

The single, giant Mauthner cell body gives rise to a single giant, heavily myelinated axon that crosses the midline and descends in the white matter column just ventral to the ventral horn. As it descends, the Mauthner axon gives off frequent collateral branches at each segment of the spinal cord. These axon collaterals have terminals directly on the primary motor neurons, which innervate the fast, white muscle fibers. The Mauthner collaterals also terminate on descending neurons that excite the primary motor neurons.

At the same time that the Mauthner cell is producing excitation of the primary motor neurons, it also produces inhibition of the corresponding primary motor neurons of the opposite side of the spinal cord by activating inhibitory commissural interneurons that cross the midline and inhibit these corresponding contralateral motor neurons. This contralateral inhibition is necessary to prevent the contraction of contralateral muscles from interfering with the sudden bending of the body into a C shape that quickly points the animal away from the direction of the threat. The relationship of the Mauthner axon to interneurons and motor neurons is shown schematically in Figure 8-5. The Mauthner cell thus serves as the heart

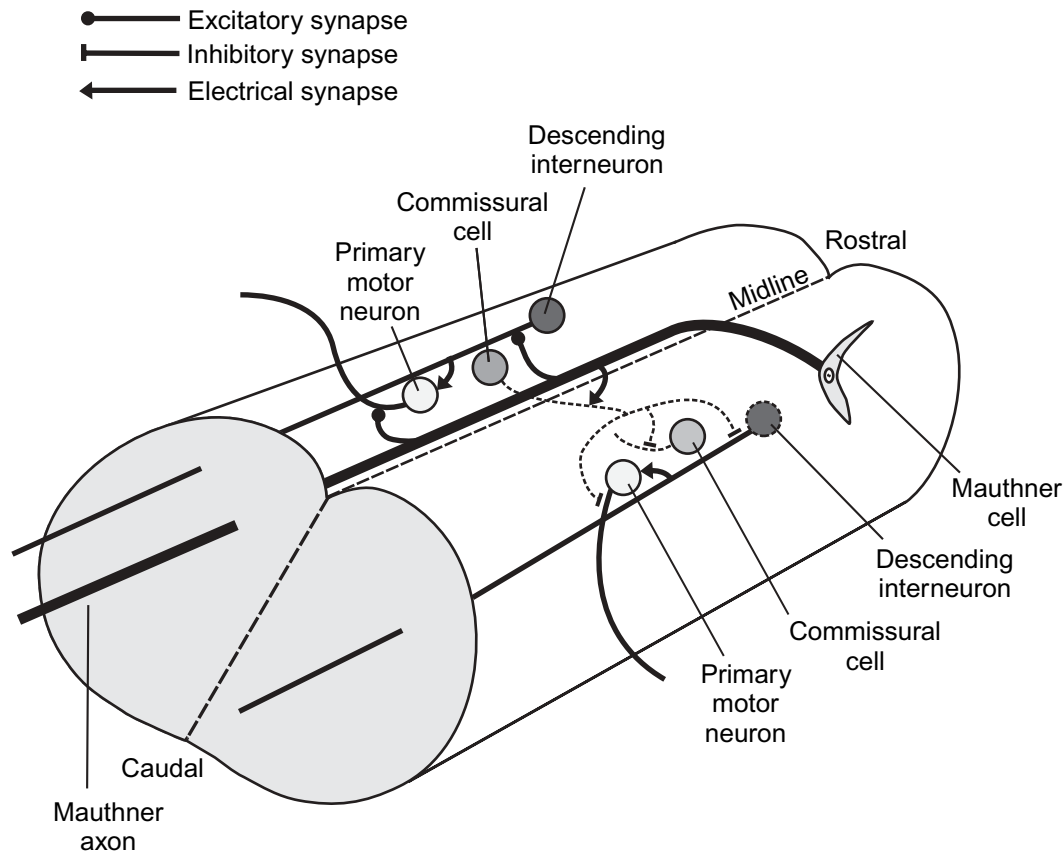


FIGURE 8-5. Pathways involved in the escape response in which the body is bent into the shape of a C. The Mauthner cell axon crosses the midline and excites both the contralateral descending interneuron and the contralateral primary motor neuron via chemical synapses. It also excites the contralateral commissural cell via an electrical synapse. The contralateral descending interneuron excites motor neurons along its path of descent toward the tail via an electrical synapse. Inhibition of the motor neurons of the side ipsilateral to the Mauthner soma is accomplished by the contralateral commissural cell, which sends its axon across the midline to the side of the Mauthner soma and inhibits the ipsilateral descending interneuron, the primary motor neuron, and the corresponding commissural cell. Adapted from Fetcho (1991).

of a powerful integrating mechanism that ensures a rapid pattern of contraction and relaxation of large numbers of muscles to result in a flexure of the body at a time when a sudden and speedy change in the direction of locomotion is required.

Until recently, amphibian Mauthner cells were thought to exist only in the animals' larval (tadpole) state and in those adult amphibian species that either remained in the water for their entire life cycle or that retained a tail in adulthood. Recent research, however, has revealed that these distinctions do not hold, and indeed Mauthner cells can be found in a wide range of amphibians irrespective of the presence of a tail or adaptation to an aquatic environment.

In tadpoles, Mauthner cells appear to play a role similar to that of their counterparts in lampreys and teleosts; that is, a sudden curvature of the body as the start of an escape reaction away from a source of threat. In animals such as frogs, however, the role of Mauthner cells is puzzling because these animals cannot flex their bodies as a fish or tadpole can, and their locomotor pattern in water is very different due to the lack of a tail, the presence of legs, and the existence of specialized muscle groups rather than myomeres. In water, escape responses in such animals consist of a sudden contraction of the body followed by movements of the legs to propel the animal in a backward direction. On land, the response to threat is an escape jump.

The Mauthner cell escape system is not the only escape system in the nontetrapod spinal cord. Several recent studies have reported that escape-like behaviors persist after destruction of the Mauthner cells. These escape-like behaviors, however, have longer latencies than in the intact animal or a lower probability of elicitation. Such observations suggest that additional neuronal systems participate in startle and escape behavior.

Electromotor Neurons

Although the term "motor neuron" typically is used to indicate efferent neurons that stimulate the contraction of muscles that move some body part, certain other neurons that are called "motor" do not actually move anything. For example, some of the visceromotor neurons of the autonomic system control the secretion of glands. Although strictly speaking they should be called "effector" neurons (indicating that they "do" something), they more often are called "motor" because of their cell type, location, or other reasons of convention. Among these effector neurons that do not move anything are the **electromotor neurons** that activate the electric organs of certain fishes. The most famous of these is the electric organs of fishes such as the electric eel, the electric catfish, and the torpedo. These electric organs, which are actually modifications of muscles, produce muscle action potentials that are so powerful they can stun prey or predators. Less well known are the weak electrical potentials, which are far too weak to stun another animal, that these animals and certain other groups of fishes produce. These weak potentials are important for social communication and for finding objects in murky waters or in dim illumination. The electrosensory system, by which these weak potentials are detected, and the ways in which they are used by these animals will be discussed in greater detail in Chapter 12. Here we will

only point out that the electromotor neurons that control these electric organs are located in a separate column of the ventral horn.

The Curious Spinal Cords of Sharks

The observant reader might have noticed that our discussion of Mauthner and Müller axons did not include sharks and related animals. These animals have the same need to make rapid escape responses as do other aquatic nontetrapods; yet for reasons that we can only speculate about, they lack the high-speed, giant axon escape systems of other nontetrapods. Their motor responses, both high-speed pursuit and escape as well as the initiation of more leisurely locomotion, are controlled by the reticulospinal, tectospinal, and vestibulospinal tracts. One might suppose that so effective a predator as a shark, which is high on the food chain, might not often need to make escape responses; this, however, is not always the case. There are often larger, more aggressive sharks to be avoided. Moreover, not all sharks are the high-speed predators that exist in the general public's image of a shark. Nevertheless, the relative freedom from predation that sharks enjoy may have played a role in the loss of the giant axon systems that characterize the spinal cords of most nontetrapods.

Ascending and Descending Pathways

Among the ascending pathways of the spinal cords of nontetrapod vertebrates is the dorsal column pathway, which consists of axons of the dorsal cells and other sensory neurons. The pathway terminates in the dorsal column nuclei, which in turn relay the sensory inputs rostrally. This pathway is present in lampreys as well as in sharks and rays and tetrapods. It appears to carry information about touch and pressure sensations from the body. A second major ascending pathway travels in the lateral columns and carries information about touch, pain, and temperature changes of the body surface to the thalamus. Other ascending pathways from the cord to the brain include the spinocerebellar, spinoreticular, and spinotectal tracts that were described in Chapter 7. In addition, ascending pathways recently have been reported from the spinal cord to the vagal and facial lobes, which are major gustatory regions of the hindbrain in teleosts (see Chapter 11).

Descending pathways are present in varying amounts depending on the development of the particular systems within the brain, such as visual, auditory, vestibular, and electrosensory. Prominent among these pathways are the vestibulospinal, tectospinal, and reticulospinal tracts. Other specialized descending pathways are trigeminospinal and gustatory-spinal. These pathways carry commands from the brain to the spinal cord, which are influenced by information acquired through the senses of the head (vision, audition, taste, vestibular sense, and electroreception). They typically end on interneurons within each segment of the spinal cord and occasionally directly on motor neurons. A descending pathway that typically is associated with the tetrapod spinal cord is the rubrospinal tract, which is one of the pathways by which the cerebellum influences motor neurons of the spinal cord. Recent studies suggest that this pathway is present in teleosts as well.

BOX 8-2. A Neuroendocrine Organ in the Spinal Cord: The Caudal Neurosecretory System

Just rostral to the ampulla caudalis, on the ventral surface of the spinal cord of elasmobranchs and holost (gars and bowfin) and teleost fishes, is an organ known as the **urophysis**, which has a number of characteristics in common with the **neurohypophysis**, or the posterior pituitary, at the base of the hypothalamus in the diencephalon, as will be discussed in Chapter 23. Both the neurohypophysis and the urophysis are endocrine organs that send their hormonal secretions into the general circulatory system. Both organs receive their neurosecretions from axons of nearby neurons. The urophysis receives neurosecretory axons from the **caudal neurosecretory nucleus**, which contains the neurosecretory **Dahlgren cells**. The Dahlgren cells secrete the hormones **urotensin I** and

urotensin II, which have been implicated in osmotic regulation, cardiovascular function, and reproduction. The main afferents to the caudal neurosecretory nucleus are by way of a serotonergic pathway from the reticular formation of the hindbrain.

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Reissner's Fiber

A feature of the ventricular system and central canal of the spinal cord is a filament-like element known as **Reissner's fiber**. The fiber begins in the **subcommissural organ**, which is one of the **circumventricular organs** (see Chapter 23 for further details), and is located ventral to the posterior commissure, which is located in the dorsal part of the mesencephalon. The fiber results from a secretion of glycoproteins by the subcommissural organ into the cerebrospinal fluid. This secretion becomes solidified into a fiber that extends caudally through the ventricular system and central canal to the **ampulla caudalis**, which is a kind of mini-ventricle at the caudal end of the central canal. Here Reissner's fiber becomes an irregularly shaped mass known as the **massa caudalis**. The massa caudalis glycoproteins do not remain in the ampulla caudalis, but instead escape through pores in the wall of the ampulla caudalis and enter a network of blood vessels at the caudal most end of the cord. The function of Reissner's fiber, which is present in all vertebrates, is unknown at present.

incoming axons as well as large numbers of motor neurons and their outgoing axons in the lumbar region. These also contribute to the lumbar enlargement. The combination of both powerful hind legs and a powerful tail, as in kangaroos and many varieties of dinosaurs (as may be seen in their fossilized skeletons), leads to an exceptionally large lumbar enlargement.

Locomotor Patterns and Spinal Cord Organization

Each of the locomotor patterns described in Chapter 7 has its representation in the local structure of the tetrapod spinal cord. In general, those segments of the cord that innervate the organs of locomotion are better developed by virtue of the presence of motor neuron pools in the ventral horns to activate the locomotor muscles, by increased numbers of neurons in the dorsal horns to receive the larger numbers of sensory neuron inputs from the locomotor organs, and by axons carrying commands from the central pattern generators. Like non-tetrapods, tetrapods also have slow-acting red muscle fibers and fast-acting white muscle fibers.

An interesting and instructive comparison that reveals the relationship between mode of locomotion and spinal cord organization can be made among three types of reptiles: alligators, snakes, and turtles. Alligators are typical of many tetrapods in that they have well-developed limb muscles, well-developed trunk muscles, and powerful tail muscles. The columns of motor neurons that supply these muscles are characteristic of most tetrapods; that is, they have a ventromedial column of motor neurons that extends along the length of the spinal cord, and lateral extensions of the ventral horns are present in the cervical and lumbar enlargements. Although they are legless, snakes nevertheless are tetrapods because they have descended from a lineage of tetrapod reptiles and, before that, tetrapod sarcopterygians. Snakes thus evolved from limbed reptiles into a body configuration that lacks external limbs, the muscles to move the limbs, and motor neurons with which to activate such muscles. Snakes, therefore, do not have ventrolateral columns of motor neurons in the cervical and

THE ORGANIZATION OF THE TETRAPOD SPINAL CORD

Like its nontetrapod counterpart, the tetrapod spinal cord contains axons entering the cord from the body interior and exterior and additionally from the limbs. Likewise, axons leave the cord to innervate the muscles and glands of the body's interior, the body's exterior, and the limbs. The axons to and from the limbs, which are one of the principal features that distinguish the spinal cords of tetrapods from their nontetrapod counterparts, are present in great numbers so that they cause the cord to bulge in the regions of their entrance and exit. Thus, the axons to and from the forelimbs produce an enlargement of the cord in the cervical region (the **cervical enlargement**) and those to and from the hind limbs result in a **lumbar enlargement**. Animals with powerful tail musculature such as alligators, beavers, and dolphins also have large numbers of

lumbar regions nor do they have cervical and lumbar enlargements. Instead, they have well-developed ventromedial columns. In contrast, turtles have more or less conventional tetrapod limb muscles but lack trunk muscles. The ventromedial cell columns are therefore very small in these animals although the ventrolateral columns are present in the cervical and lumbar regions. A similar situation exists in the spinal cords of birds. Finally, in mammals such as primates and raccoons, which have exceptional ability to manipulate objects with the digits of their forelimbs (hands), the ventrolateral columns of motor neurons are more elaborate than in other tetrapods.

Figure 8-6 shows a schematic representation of three types of spinal cords. At the left is a typical tetrapod spinal cord with cervical and lumbar enlargements and a thick thoracic region. The center diagram shows a snake spinal cord that lacks cervical and lumbar enlargements because of the lack of limbs, but which is thick throughout its length due to the powerful trunk musculature that is the basis of the animal's locomotion. At the right is the type of spinal cord that is characteristic of turtles and birds. It has lumbar and cervical enlargements due to the limbs of these animals, but the spinal cord is thin in the thoracic region. In the case of turtles, the thinness is due to the lack of trunk musculature in the thoracic and abdominal regions, which are contained within the armored shell of the animal. Thus, the sensory input to these levels is mainly visceral. The thin thoracic cord of birds derives from the lack of necessity to coordinate the actions of the hind limbs and forelimbs. When birds fly, their feet are neatly tucked flat against the body; when they walk, their wings are firmly positioned against the body. One can readily see the lack of coordination between the forelimbs and hind limbs of birds when observing a chicken running from a threat. Its wings flap and its legs run, but there seems to be little coordination between the two, which results in a rather clumsy escape. This contrasts sharply

with the very smooth, precise, and rhythmic patterns that exist when birds walk or fly.

The Curious Spinal Cords of Birds

One of the more dramatic examples of how locomotor patterns affect spinal cord morphology may be seen in the lumbar region of the avian spinal cord. Birds, like other tetrapods with well-developed hind legs, have a well-developed lumbar enlargement. Unlike other tetrapods, however, the dorsal white and gray columns have separated in the caudal lumbar and sacral regions to form a cavity known as the **lumbosacral sinus** or **rhomboid sinus**. This cavity appears to have been formed as a consequence of the extremely large avian sciatic nerve, which is formed by nerve roots from several segments in this region and which is the main sensory and motor nerve of the leg. The cavity, however, is not a ventricle of the central nervous system as is the fourth ventricle of the brain, which contains cerebrospinal fluid. The central canal, which contains the cerebrospinal fluid, passes, like a water pipe suspended in air, through the lumbosacral sinus rather than opening into it as in the case of the fourth cerebral ventricle. The lumbosacral sinus is illustrated in Figure 8-7.

The lumbosacral sinus is not empty, however; it contains a large gelatinous mass that surrounds the central canal. This mass, which is rich in glycogen, is known as the **glycogen body**. Glycogen is a stored form of glucose, typically found in the liver, which is vital for the nutrition of body cells. More modest glycogen stores have been found along the length of the central canal extending as far rostral as the medulla. The functions of the glycogen body have been the subject of much speculation. Perhaps the most plausible explanation at present is the suggestion that this storehouse of glycogen may play a

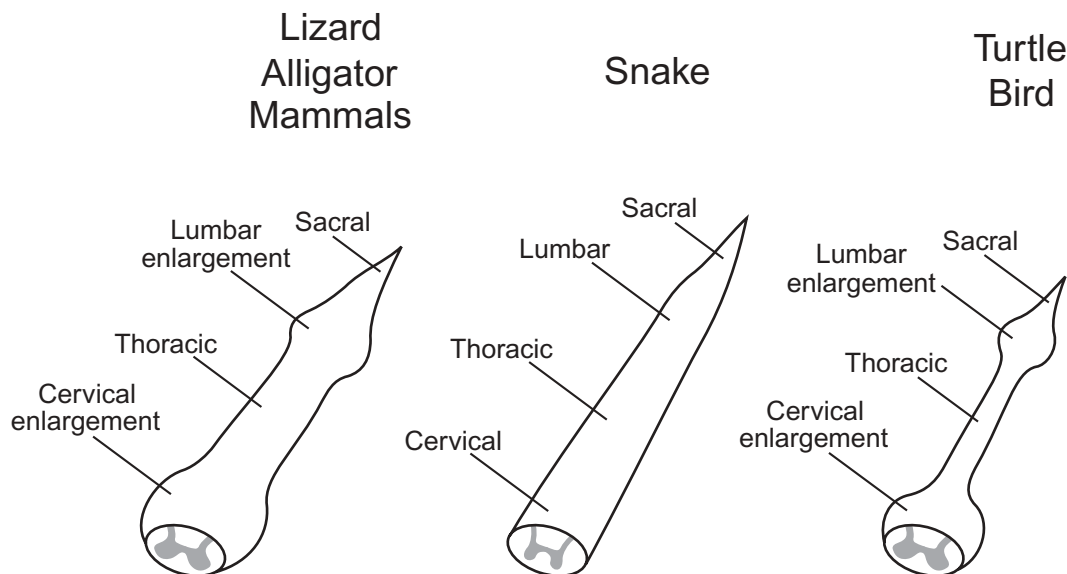


FIGURE 8-6. Schematic representations of three types of spinal cord. Left: Typical tetrapod spinal cord with cervical and lumbar enlargements and a thick thoracic region. Center: A snake spinal cord that is thick throughout its length and lacks cervical or lumbar enlargements. Right: A spinal cord characteristic of turtles and birds that has cervical and lumbar enlargements but is thin in the thoracic region.

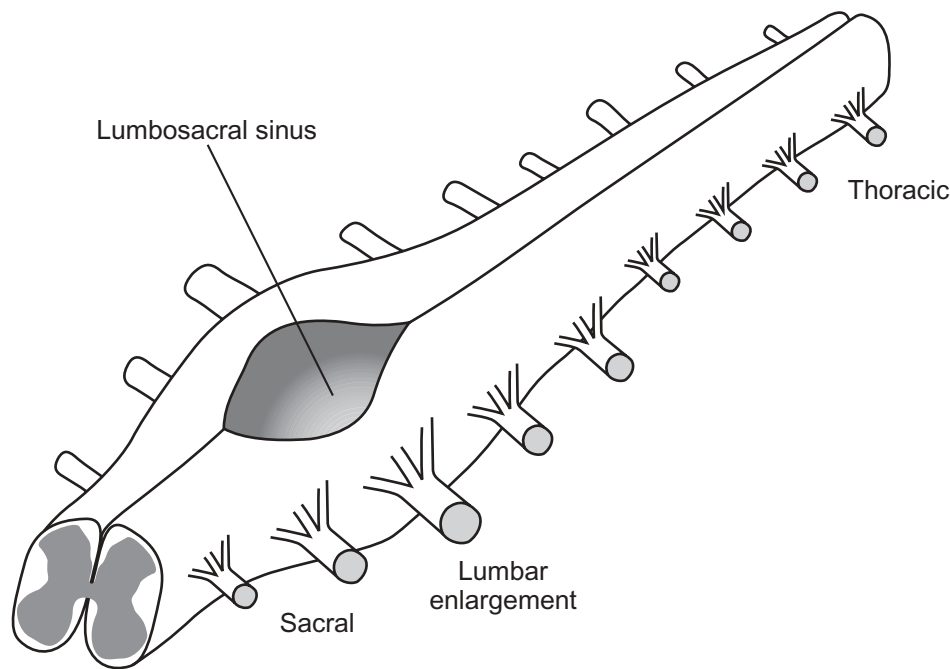


FIGURE 8-7. A pigeon lumbar cord showing a large cavity, the lumbosacral sinus, located within the lumbar enlargement. The glycogen body (not shown) fills this cavity.

role in the formation of myelin during development and may serve as an alternative source of energy for the central nervous system during periods of high metabolic stress. A recent report suggests that the glycogen body may supply substances to the brain via the cerebrospinal fluid circulation.

Glycogen bodies also occur in the spinal cords of the embryos of mammals and have been reported in adult newts. The presence of the glycogen body in the lumbosacral sinus may not have anything in particular to do with the lumbar region of the spinal cord, but rather may be a chance occurrence that took advantage of an unrelated evolutionary development.

Segmental Organization

In addition to entering sensory axons and motor neuron cell bodies and their exiting axons, the tetrapod spinal cord contains a large number of intermediary neurons. Many of these are intrasegmental interneurons, and their axons remain within their spinal segment. Others are extrasegmental and send their axons to one or more additional segments. Many of these extrasegmental neurons send their axons beyond the spinal cord to targets located in the brain such as sensory nuclei of the medulla as well as the cerebellum, the thalamus, and the reticular formation. These brain structures are components of complex brain systems that control the activities of the spinal cord by means of descending axonal pathways from the brain to the spinal cord, including the reticulospinal, tectospinal, vestibulospinal, rubrospinal, cerebellospinal, and hypothalamospinal pathways. These large numbers of ascending and descending axons result in a progressive increase in the diameter of the spinal cord from caudal to rostral as each succes-

sive segment makes its contribution to or receives its contribution from the traffic with the brain.

Lamination

When considered from a longitudinal perspective, the gray matter of the tetrapod spinal cord is organized into continuous columns of neurons. The spinal cord, however, also can be viewed in a transverse or segmental perspective. When we consider a transverse section through any spinal segment, the intermediary neuron and motor neuron cell columns can be viewed as forming laminae (layers) beginning in the dorsal horns and continuing ventrally into the ventral horns. This approach to the cytoarchitecture of the spinal gray matter was first proposed by the Swedish anatomist, Bror **Rexed**, who recognized nine laminae in the cat spinal cord. His system has since been shown to be applicable (with some minor variations) to the organization of the spinal cords of nearly all tetrapods. Figure 8-8 shows some examples of this cytoarchitectonic organization in a lizard, a pigeon, and a human.

Each lamina consists of cells of a particular type. Many of the laminae are present in transverse sections through neuronal cell columns that extend for most or all of the cord's length, whereas others consist of cell groups that exist only at specific levels of the cord, such as the cervical and lumbar enlargements; thus, not all laminae are present in each spinal segment. Although the laminae vary somewhat in form from region to region of the spinal cord, a more or less consistent pattern can be observed throughout. Laminae I–VI form the dorsal horns. The cells of these laminae are the neurons that are the sources of the ascending pathways to the brain as well as intrasegmental and extrasegmental spinal pathways.

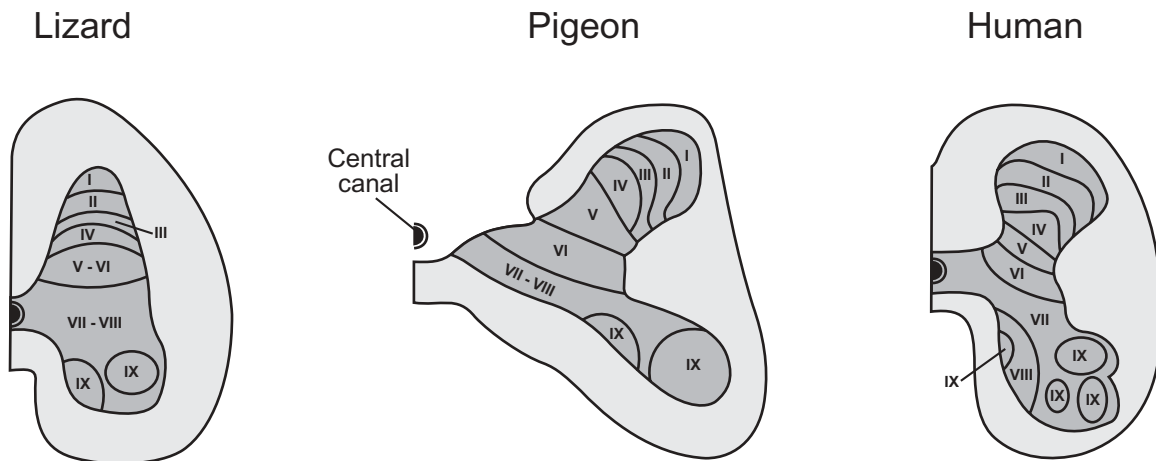


FIGURE 8-8. Lamination in the gray matter of three tetrapods: a lizard, a pigeon, and a human. Laminae I–VI constitute the dorsal horn. Laminae VIII and IX are the ventral horn. Many axons of descending pathways terminate in lamina VIII. Lamina IX neurons are the motor neurons.

Lamina VII forms an intermediate zone between the dorsal and ventral horns. In addition to being a principal contributor to the spinocerebellar pathways, lamina VII is also involved in the autonomic system. At its medial edge is a column of cells known as the **intermediomedial column**; these cells are the targets of the visceral sensory (visceral afferent) axons. At its lateral edge, in the lateral horn of the thoracic and lumbar regions, is the **intermediolateral column** that contains the preganglionic neurons of the sympathetic division of the autonomic nervous system. The intermediolateral column is present only in the thoracic and lumbar regions, and its preganglionic axons project to the sympathetic ganglia located on the ventral roots of the spinal cord. Postganglionic axons travel to various internal organs of the body (collectively known as the viscera) and produce contractions of smooth muscles such as those of the intestinal system or stimulate the secretion of glands. The sympathetic division of the autonomic nervous system, along with the parasympathetic division, will be discussed in greater detail in Chapter 23.

Lamina VIII is a major coordinating zone of the gray matter. It contains interneurons that are the targets of many of the descending pathways from the brain and other levels of the spinal cord. These interneurons coordinate both reflex and voluntary commands from the brain with reflex actions of the spinal cord.

Lamina IX consists of separate groups of cells that form the motor neuron columns that innervate the muscles of the skeleton. In the regions of the spinal enlargements, the groups of lamina IX cells are larger and better developed than elsewhere.

Intrinsic Spinal Neurons

After passing through the dorsal white matter via a region known as the **zone of Lissauer**, incoming axons from pain and temperature receptors at the body surface as well as from receptors on the visceral surfaces of the body enter the gray matter of the cord. These axons terminate on neurons in laminae I and II. Lamina I is important in the processing of pain.

Lamina II is also known as the **substantia gelatinosa** and takes its “gelatinous” appearance from the presence of large numbers of lightly myelinated and unmyelinated axons as well as many dendrites. The axons of the lamina II neurons belong to the intrinsic spinal system; that is, they terminate within their own segment or travel to other spinal segments but they do not project to the brain. These neurons may modulate or “gate” sensory information entering the spinal cord. Laminae III and IV neurons also are mainly intrinsic to the spinal cord, although some lamina IV axons form part of the **spinothalamic** system. The neurons of lamina V, which is present only in the cervical and lumbar enlargements, receive incoming axons from limb muscles as well as axons from descending spinal pathways. In general, a somatotopic map of the innervated body region is present in the dorsal horn. An unusual feature, however, has been reported for the avian dorsal horn: two, nonoverlapping body maps in laminae II and III.

Lamina VIII interneurons coordinate reflex actions such as spinal reflexes and vestibulospinal reflexes, as well as cerebellospinal functions (via the rubrospinal tract) and voluntary movements via the reticulospinal route, and, in some cases, direct telencephalic pathways to the spinal cord.

Somatotopic Organization of the Ventral Horns

As illustrated in Figure 8-9 in a primate cervical spinal cord, the motor neuron cell columns that we would encounter as we progress from medial to lateral across the ventral horn are those that innervate the muscles of the trunk (most medial), then those that innervate the shoulder muscles, then the upper arm muscles, then the forearm muscles, and finally those motor neuron columns that innervate the muscles of the hand (most lateral). This representation of the body parts in the nervous system in the same sequence as they exist in the body is known as a **somatotopic organization**. We will encounter somatotopic body “maps” elsewhere in the motor system as well as a number of places in the somatosensory system. A second type of organization also exists in the ventral horn; the more dorsal

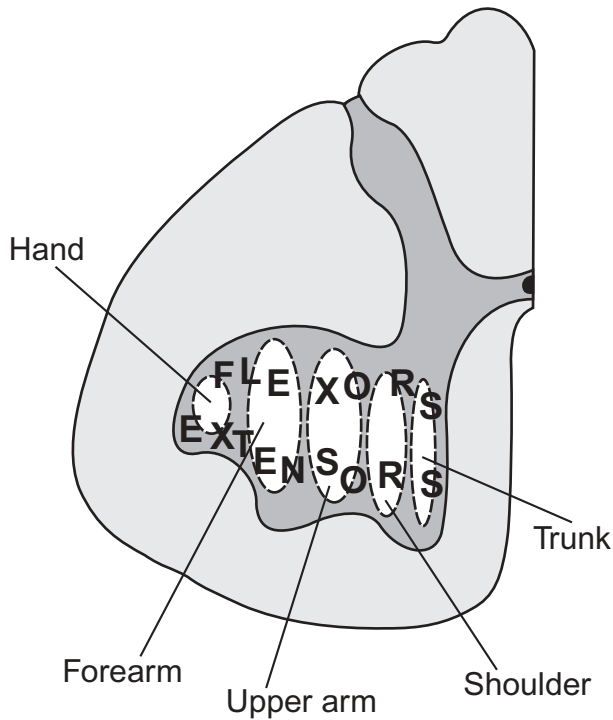


FIGURE 8-9. Somatotopic organization of the motor neuron pools of the ventral horn that control the forelimb. The spatial distribution of motor neurons in the ventral horn corresponds to the spatial distribution of the body parts that they control. Thus, those motor neurons that control trunk muscles are located most medially in the horn, those that control the arm muscles are intermediate in the horn, and those that control the hand or paw are most lateral. Those motor neurons that control flexor muscles are located in the dorsal part of the horn; those that control extensor muscles are located ventrally.

motor neuron columns innervate the flexor muscles of the trunk, shoulder, upper arm, forearm, and hands while the more ventral motor neuron columns innervate the corresponding extensor muscles.

Renshaw Cells

In our discussion of the Mauthner cell earlier in this chapter, we encountered the concept of the recurrent collateral. These small side branches that “flow back” toward the cell body are typical of motor neurons in the spinal cords of mammals. Recurrent collateral branches terminate on small, inhibitory neurons called **Renshaw cells**. Figure 8-10 illustrates a motor neuron with its recurrent collateral and associated Renshaw cell. The Renshaw cell, in turn, sends its axon with its inhibitory terminals to the cell body of the very axon from which the recurrent collateral originated (recurrent inhibition). When the action potential sweeps down the axon toward the terminal in the muscle, it also travels in the recurrent collateral and excites the Renshaw cell. The Renshaw cell then inhibits the cell body. In other words, when the motor neuron is activated, it triggers a mechanism that results in its own inhibition. As in the case of the Mauthner cell’s recurrent

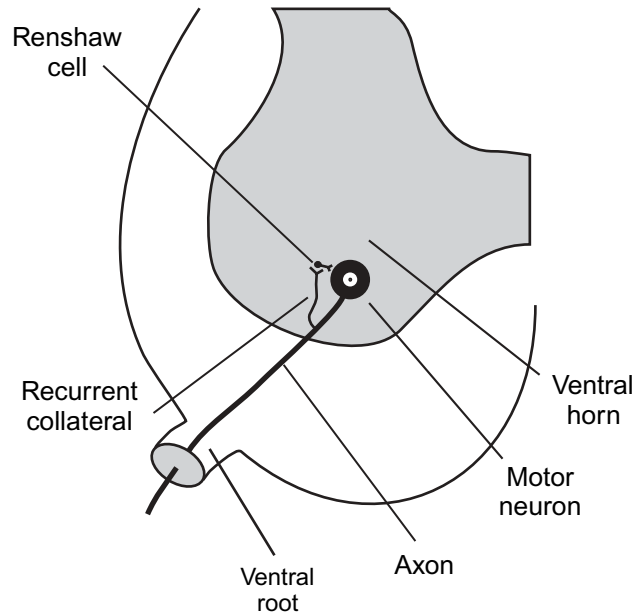


FIGURE 8-10. Recurrent inhibition via a Renshaw cell in the ventral horn of a mammal’s spinal cord. The efferent axon of the motor neuron sends a recurrent collateral branch back toward the soma where it excites a Renshaw cell, which in turn inhibits the motor neuron.

inhibition, the Renshaw cell inhibition results in the stimulation of the muscles being in the form of discrete pulses. Although a few examples of recurrent inhibition have been reported in nonmammals, we have been unable to find any reports of Renshaw cells in any vertebrates other than mammals.

Axon Columns and Cell Columns

Like the nontetrapod spinal cord, the tetrapod spinal cord consists of longitudinal columns of ascending and descending axons (the white matter) that surround a core of longitudinal columns of cells (the gray matter). Unlike nontetrapods, in which the gray matter shows considerable variation in shape, the spinal gray matter of many tetrapods shows a remarkable consistency in shape. The dorsal and ventral horns of the right and left side are connected by a small bridge of gray matter that gives the gray matter the overall form of a letter H when viewed in transverse section. In the cervical and lumbar enlargements, however, the ventral horns extend laterally so that in these regions the gray matter takes on the shape of a butterfly. Also present in the thoracic and lumbar regions of mammals are small lateral extensions of the gray matter, just above the ventral horns; these are the lateral horns.

In general, the dorsal horns consist of the cell bodies of neurons that are the sources of ascending (and some descending) axons of the white matter columns (extrasegmental axons) as well axons that remain within the spinal cord segment (intra-segmental axons). Among the dorsal horn cells are those that are the sources of the long axon pathways from the spinal cord to the brain, such as the spinothalamic and spinocerebellar

tracts, as well as some of the spinocerebellar tract components. The ventral horns contain columns of motor neurons, the axons of which pass out of the spinal cord via the ventral roots. The most medial column consists of somatic motor neurons that terminate on the muscles of the body trunk; that is, the muscles of the back, the chest, the abdomen, and to some extent, the muscles of the neck. This medial cell column of the ventral horn (the ventromedial column) is present along the entire extent of the spinal cord. In the cervical and lumbar regions, the ventral horns expand laterally to accommodate the presence of the somatic motor neurons that send their axons to the muscles of the limbs. These lateral extensions are the ventrolateral columns. In the lumbar region, the ventral horns also contain neurons that give rise to spinocerebellar tract components.

Marginal Cells

Not all of the neurons of the spinal cord are located in the central cell columns. A small column of scattered cell bodies is located along the outer margin of the spinal cord in the lateral column of white matter. These cells, known as **marginal cells**, are found in mammals, reptiles, and birds, and, among the non-tetrapods, they are found in lampreys and elasmobranchs. They form a continuous column along much of the spinal cord. These marginal cells have a number of characteristics in common with mechanoreceptors (cells that respond to stretching, mechanical bending, or deformation). They are in contact with the **denticulate ligaments**, which are filaments of connective tissue that run lengthwise along the outside of the cord between the dorsal and ventral roots. These filaments are joined to the dura mater (the outermost and toughest of the series of membranes that envelop the central nervous system) by a series of tooth-like (and hence the name “denticulate”) triangular attachments. The denticulate ligaments appear to provide mechanical support for the spinal cord. The anatomy and some physiological evidence suggest that the marginal cells are intraspinal mechanoreceptors that respond to flexing or bending of the spinal cord as the animal twists or bends its body. These cells may play a role in providing sensory feedback during rhythmic movements.

Accessory Lobes

In birds, the marginal cell column moves outside of the margins of the cord in the lumbar region to form a series of small **accessory lobes** on the outer surface of the spinal cord, but within the vertebral canal in which the cord runs. The neurons within these lobes are embedded in clusters of glycogen cells, similar to those of the glycogen body. The neurons of the accessory lobes are cholinergic. The lobes also give evidence of the presence of glutamate, glycine, and GABA. These are also characteristics of the marginal cells. Like the marginal cells, the accessory lobes appear to play a role in mechanoreception of body movements.

Ascending Spinal Pathways

In general, the dorsal horns contain the cells of origin of some ascending pathways that carry somatosensory informa-

tion to the brain. For example, lamina I neurons, in addition to some axons from laminae IV and V, are the sources of the **spinothalamic axons**. These axons carry information about touch, pain, and temperature to the somatosensory region of the dorsal thalamus. These laminae also contain neurons that send their axons to the tectum of the midbrain, via the **spino-tectal pathway**. The close association of this pathway with the spinothalamic pathway suggests that it may be carrying similar information to the tectum, which coordinates visual and auditory information with somatosensory information.

The neurons of lamina VII, along with some cells of laminae V and VI, are the source of the spinocerebellar axons. Within lamina VII is a distinctive group of cells, sometimes known as **Clarke's column**, that gives rise to the **dorsal spinocerebellar tract**. The axons of other lamina VII neurons join axons originating in laminae V to VIII to form the **ventral spinocerebellar tract**. Closely related to the spinocerebellar pathways are the **spino-olivary pathways** that terminate in the inferior olivary nuclei located at the junction of the medulla and pons. This complex of nuclear groups has reciprocal connections with the cerebellum as well as other components of the sensory and motor systems.

Lamina V neurons are the spinal cord component of the reticular formation. They participate in local reflexes and are the source of the spinoreticular pathway to the cell groups of the reticular formation in the medulla, pons, and midbrain tegmentum.

Not all ascending pathways originate from neurons of the spinal cord. Some are made up of direct dorsal root fibers. These axons are branches of incoming sensory neurons; one branch terminates near the segment of entry, whereas the other enters the dorsal white matter column and ascends to the caudal end of the medulla where it terminates in one of two groups of neurons, known as the **dorsal column nuclei**. In mammals the dorsal column is divided into two segments: a medial segment (**fasciculus gracilis**), which is present throughout the cord, and a lateral segment (**fasciculus cuneatus**), which is present only at the thoracic and cervical regions. The dorsal column nuclei are therefore also known as the **nucleus gracilis** and the **nucleus cuneatus**. The cells of the dorsal column nuclei send their axons to the somatosensory region of the dorsal thalamus by a major ascending sensory pathway known as the **medial lemniscus**. The dorsal column-medial lemniscus system carries information about pressure on the body surface, the ability to recognize the shape of an object that touches the body surface, the ability to discriminate the touch of one point from two, as well as proprioception (position sense). Additionally, the accessory cuneate nucleus relays upper limb inputs to the cerebellum.

Descending Spinal Pathways

The brain exerts its control over the spinal cord by means of a group of descending pathways. These pathways control voluntary and reflex movement and muscle tone as well as influencing visceral activity and the transmission of somatosensory information within the spinal cord.

Among the brain regions that control involuntary or reflex movements are the cerebellum and the vestibular nuclei. The vestibular nuclei receive information about gravity and accel-

BOX 8-3. Sexual Dimorphism in the Spinal Cord

Sexual dimorphism, which refers to morphological differences between males and females of the same species, is being reported with increasing frequency at various levels of the brain and spinal cord. Spinal cord motor neuron groups that serve the copulatory muscles, known as the **nucleus of Onuf**, typically have a greater number of cells in males than in females. This difference is due to the presence of androgens in the developing male. Initially, both sexes have the same number of cells, but in the females the lack of androgens results in the death of a considerable number of cells by a process known as **apoptosis** or **programmed cell death**. This sexual dimorphism has been described in mammals, including humans, and recently in green anole lizards (*Anolis carolinensis*).

Another example of sexual dimorphism in the spinal cord was described in golden-collared manakins (*Manacus vitellinus*), which are forest-dwelling birds from Panama. The male birds engage in elaborate courtship displays that

involve the use of their wings and legs. The motor neuron groups in the cervical and lumbar enlargements that control the birds' wing and leg muscles accumulate more testosterone in males than in females.

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eration from the semicircular canals of the middle ear. The cerebellum receives information from the vestibular system, from the spinal cord via the spinocerebellar pathways, and from the motor system of the cerebrum. Together with the cerebellum, the vestibular nuclei control muscle tone, balance of the body, and the coordination of the actions of the musculoskeletal system. The vestibular nuclei directly influence the spinal cord by means of the **vestibulospinal tract**. Vestibulospinal reflexes maintain body posture and balance as the body changes its rate of acceleration or suddenly encounters an uneven surface during locomotion. The cerebellum, which influences muscle tone and coordination of postural reflexes, has both direct and indirect links to the spinal cord. The direct input to the spinal cord is via the **cerebellospinal tract**, which originates in the **deep nuclei of the cerebellum**. It is only a minor input, however, and is restricted to the cervical part of the cord. Of the indirect routes, one is via the vestibular nuclei. The major route of cerebellar influence on the spinal cord is also indirect via a specialized component of the mid-brain reticular formation known as the **nucleus ruber** or the **red nucleus**. The efferents of the red nucleus are known as the **rubrospinal tract**, which is a pathway characteristic of animals that use their limbs for locomotion. Although they typically are most prominent in land vertebrates and their descendants, a red nucleus and rubrospinal tract also have been reported in a ray (*Raja clavata*) that uses its pectoral fins to "fly" through the water much as a bird flies through the air, as well as in squalomorph sharks, gars, teleosts, and lungfishes.

Somatosensory cell groups of the brainstem also contribute to the descending spinal pathways. The dorsal column nuclei as well as those cell groups that receive somatosensory information from the head send their axons (**trigemino-spinal**) to the spinal cord. These pathways permit body movements in response to touch stimuli on the head or body.

The control of voluntary movement is carried out by several descending pathways, and the pattern of pathways varies among tetrapods. A common component of these descending motor pathways is the **reticulospinal system**. The reticulospinal pathways are the main means by which the brain controls and coordinates voluntary movement of the body parts in most tetrapods. Pathways originating in motor regions of the telencephalon send their axons to the **lateral** and **medial reticular formation** of the caudal brainstem. The medial reticular formation and the lateral reticular formation are the sources of the reticulospinal tracts. These tracts terminate mainly on neurons in laminae VII and VIII of the ventral horns and occasionally on motor neurons of lamina IX.

In addition to the reticulospinal pathways, mammals possess a direct pathway from the cerebral cortex of the telencephalon to the spinal cord, which is known as the **corticospinal tract** or **pyramidal tract**. This pathway leaves the telencephalon and passes through the brainstem to the caudal medulla where most of the axons decussate (cross the midline) and descend in the contralateral spinal cord as the lateral corticospinal tract; a smaller portion of these corticospinal axons remain ipsilateral (anterior corticospinal tract). An exception to this rule may be seen in moles and hedgehogs, in which the corticospinal tract remains entirely ipsilateral.

The axons of the corticospinal tract do not extend the full length of the spinal cord in all mammals. In marsupials, for example, the corticospinal axons extend no further than the cervical or anterior thoracic levels. However far they extend, some of these axons terminate on interneurons of laminae VII and VIII of the ventral horn, although many terminate directly on motor neurons of lamina IX.

The decussation of the corticospinal tract often is regarded as the boundary between the caudal medulla and the rostral spinal cord. In the echidna or spiny anteater, which is

a monotreme, and in some bats, the crossing occurs in the rostral medulla. In many mammals, such as primates, carnivores, and rabbits, the crossed corticospinal tract travels in the lateral columns of white matter and the uncrossed travels in the ventral white matter columns. In other mammals, however, such as rodents, the corticospinal axons are found in the dorsal white matter columns between the dorsal horns.

The corticospinal tract is relatively small in monotremes (the platypus and spiny anteater) and marsupials. It is somewhat better developed in placental mammals and is particularly well developed in those placentals that manipulate objects with the digits of their forepaws or hands such as rodents, raccoons, and primates.

Direct axons of cortical neurons that pass to the gray matter of the spinal cord generally have been regarded as an exclusive feature of mammals. Although reports of a pathway from the telencephalon to the spinal cord in birds have been made since the early 20th century, the notion persists in the mammalian literature that only mammals have a corticospinal (pyramidal) tract. Studies of birds, however, indicate that axons originating in the telencephalon follow a course through the brainstem that is remarkably similar to the corticospinal tract of mammals. These axons terminate in the ventral horn of the cervical region of the spinal cord. Among the avian species in which corticospinal-like pathways have been reported are parrots, owls, pigeons, ducks, and finches.

The midbrain tectum, with its maps of visual and auditory space as well as a body map, is the structure responsible for the involuntary reflex turning of the head in the direction of the source of a stimulus, as happens when a sudden and unexpected visual or auditory stimulus occurs. Efferent axons of the tectum form the **tectospinal tract**, which ends on interneurons of the ventral horn in the cervical region. These interneurons in turn activate motor neurons that control the appropriate head and neck muscles to carry out this orientation response.

Just as the somatic motor system is controlled by the brain, the visceral motor or autonomic system is also under control of the brain. Descending axons from the hypothalamus (**hypothalamospinal tract**) and visceral cell groups (**solitariusospinal tract**) in the medulla terminate on the preganglionic neurons of the sympathetic division of the autonomic nervous system that are located in the intermediolateral column or lateral horn of the spinal cord.

Tetrapod Central Pattern Generators

The execution of the complex patterns of contraction and relaxation of limb and trunk muscles that produce various locomotor patterns and other rhythmic movements of body parts is under the control of central pattern generators, which are interneuron networks located within the spinal cord, mainly in laminae VII and VIII, and in the brainstem. These networks coordinate and synchronize the actions of motor neurons on the left and right sides of the spinal cord to produce a smooth, locomotor progression of the body across the land, through the water, or through the air. Initiation of the actions of the central pattern generators of the spinal cord is controlled by interneuron networks located in the lateral reticular formation of the caudal brainstem, known as **command generators**. These

command generators influence the central pattern generators of the spinal cord by means of reticulospinal pathways.

EVOLUTIONARY PERSPECTIVE

The spinal cord has remained relatively stable in its evolution. Its basic functions of gathering sensory information about touch, deformation of body surfaces, pain, and temperature from the external and internal environments and executing reflex actions in response to this sensory information, have remained relatively unchanged throughout vertebrate history. What has varied in spinal cord evolution has been the shift from body undulation and tail propulsion (with some assistance from fins) as the means of locomotion in aquatic animals to rhythmic movements of limbs for locomotion in tetrapods. These changes are seen in the development of regional concentrations of sensory neurons, motor neurons, and intermediary neurons to serve these organs and their functions, the development of the cell columns that give each spinal segment its laminar organization, and the development of somatotopic organization within these laminae. In concert with these changes, an increased communication between the spinal cord and the hindbrain and forebrain is reflected in the increased development of long ascending and descending pathways not only for control of rhythmic movements of limbs but also for the voluntary initiation of movement patterns.

When flight developed in certain mammals, reptiles, and birds, hindlimb locomotion in these animals became separated from forelimb locomotion. The latter were used almost exclusively for flight, whereas the former were used only for walking, hanging, clinging, and limited manipulation of objects. This reduced coordination between forelimbs and hindlimbs is reflected in the overall form of the spinal cord. In those mammals that have the ability to adroitly use the digits of their limbs, manipulation of objects in the environment is an important aspect of their survival. The ability to dig, to pick up and displace objects, to manipulate food objects as they are eaten, and to modify their environment in other ways is reflected in the greater development of long descending pathways from the cerebrum to the motor neuron groups that control the limbs and digits. Similar pathways may be seen in birds, which also manipulate objects with their hindlimbs (although their primary organ for manipulation is the bill), and to a lesser extent in reptiles.

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Segmental Organization of the Head, Brain, and Cranial Nerves

“TWELVE” CRANIAL NERVES

Traditionally, 12 cranial nerves have been recognized, and the list of them, numbered with Roman numerals, has been taught to many generations of students. The nerves have been named according to various attributes, such as their appearance (vagus = wanderer), the region of innervation (facial), or their function (oculomotor = moving the eye). A list of the traditionally recognized 12 cranial nerves is shown in Table 9-1. This list is useful for the study of human neuroanatomy, for which it was devised, but it is inadequate for the comparative neuroanatomy of all the vertebrate classes. There are, in fact, many more than 12 cranial nerves. The terminology used in this text for all of the cranial nerves preserves the original Roman numeral designations of the “traditional” 12. These designations are so firmly established in the literature and so universally used that changing to a new set of numbers would be counterproductive.

Some of the cranial nerves have only one component, whereas others have as many as five. As is the case for the spinal nerves, the sensory components of the various cranial nerves (with the important exception of the optic nerve) have their bipolar neuron cell bodies in the peripheral nervous system (see Chapter 2). These cells are derived from two tissues that lie near but not within the neural tube during embryological development (see Chapter 3)—neural crest and placodes. The bipolar neuron cell bodies are grouped within ganglia that lie near the brain, and their axons project into the central nervous system. There they terminate on groups of multipolar (Golgi Type I) neurons within the hindbrain or the telencephalon, which in turn will project to other groups of multipolar

neurons. Hence, the sets of multipolar neurons that receive the bipolar neuron afferent projections are referred to here as first-order multipolar neurons, or FOMs, for convenience (see Chapter 3). The motor cranial nerves either project directly to the muscles that they innervate, with only the distal portions of their axons extending beyond the brain and into the periphery, or they project to other motor neurons that lie within ganglia of the peripheral nervous system. The latter neurons are derived from neural crest, and they project in turn to the target muscles or glands. The latter, two-neuron chain type of arrangement is for components of the parasympathetic nervous system (see Chapter 3).

Traditionally, the components of the cranial nerves have been classified according to three parameters. One parameter is whether they innervate somatic (body wall) or visceral (associated with the gut) organs. Another parameter is their function, i.e., whether they are afferent (meaning sensory in this context) or efferent (motor). The third parameter is an assignment of “general” or “special” to the nerve component. As introduced in Chapter 3, the somatic-visceral and afferent-efferent parameters are sufficient to completely describe all four components of the spinal nerves. The “general” parameter is additionally assigned to all spinal and some of the cranial nerve components only to distinguish them from the “special” cranial nerve components. The spinal nerve components (in dorsoventral order) are 1) general somatic afferent (GSA), 2) general visceral afferent (GVA), 3) general visceral efferent (GVE), and 4) general somatic efferent (GSE). The traditionally used category of “special” for some cranial nerve components was assigned in the mistaken belief that these components were different in some way from the general components. On the sensory side, the categories of “special somatic afferent” (SSA) and “special

TABLE 9-1. The Traditional Twelve Cranial Nerves

Symbol	Name	Innervation
I	Olfactory	Olfactory epithelium
II	Optic	Retina
III	Oculomotor	Internal and external eye muscles
IV	Trochlear	External eye muscles
V	Trigeminal	Jaw muscles; touch to face, snout and oral cavity
VI	Abducens	External eye muscles
VII	Facial	Taste buds; facial muscles; salivary and tear glands
VIII	Vestibulocochlear	Cochlea, vestibular organs
IX	Glossopharyngeal	Taste buds; pharynx; salivary glands
X	Vagus	Taste buds; viscera of thorax and abdomen; larynx; pharynx
XI	Spinal accessory	Neck and shoulder muscles; larynx
XII	Hypoglossal	Tongue

visceral afferent” (SVA) have been used. For some motor components, the category of “special visceral efferent” (SVE) has been used.

In contrast, the so-called “general” sensory modalities for touch, position sense, pain, and temperature in the head were recognized correctly as corresponding to the same modalities for the body and thus categorized as general somatic afferent (GSA). Likewise, the sensory input from the viscera was categorized as general visceral afferent (GVA). The senses listed as “special somatic afferent” (SSA) vary from one author to another but always include the components of the eighth cranial nerve for vestibular sense (balance) and hearing, and the lateral line nerves (for mechanoreception and electroreception) of nontetrapod vertebrates belong in this category as well. The olfactory nerve and other senses of the telencephalon (vomeronasal and terminal nerves) and light-receptive (optic and epiphyseal nerves) are often unclassified but sometimes added to the SSA category. The “special visceral afferent” (SVA) category is reserved for the taste components of three nerves of the hindbrain. As we will discuss below, the notion that the “special” senses were different in some manner from the general senses has been refuted by recent findings of common embryological origin of the bipolar sensory neurons for the general and special (nonvisual) components alike.

On the motor side, the general somatic efferent (GSE) category was correctly assigned to the cranial nerve components that innervate the extraocular muscles and the muscles of the tongue. Likewise, the general visceral efferent (GVE) category was correctly assigned to the parasympathetic components of several cranial nerves, which innervate the intraocular muscles and the lacrimal and salivary glands and provide parasympathetic innervation to most of the viscera. The so-called “special

visceral efferent” (SVE) category was assigned to the cranial nerve components that innervate the muscles of the jaws, face, and throat (gill) region. This category is sometimes also applied to the muscles that turn the head and lift (shrug) the shoulder. As we will discuss below, these muscles were erroneously believed to be visceral in nature, but their nerves were classified as “special” due to the paradox of the somatic histological characteristics and voluntary control of these muscles.

The work of Drew Noden, beginning in the early 1990s and since corroborated and expanded on by him and other developmental biologists, has demonstrated that the perceived differences are not valid: the “special” category is no longer useful and, worse, it is highly misleading. The simple fact is that the classification of most cranial nerve components can be reduced to the same four categories as used for spinal nerve components—somatic afferent, visceral afferent, visceral efferent, or somatic efferent. The only exceptions to this principle are the two visual cranial nerves (optic and epiphyseal), which are derivatives of the neural tube and thus parts of the central nervous system itself. Essentially, the use of the term “special” in reference to any cranial nerve component can now be interpreted—with the great advantage of hindsight—as meaning that it was not correctly understood and that it did not make sense! In dropping the category of “special,” that of “general” becomes superfluous and can likewise be discarded. The resolution is that the situation is much simpler than was ever before appreciated: all nonvisual components are either sensory (afferent) or motor (efferent) and their innervation is either of the body wall (somatic) or is visceral. If you keep this simple view in mind as you deal with them, you will be able to better resist the confusion that has been created.

THE VERTEBRATE HEAD: SEGMENTAL ORGANIZATION

Understanding the organization of the cranial nerves and the rationale for their classification depends on an appreciation of the segmental nature of the brain and head and of the embryonic derivation of the nerves, their ganglia, and the structures that they innervate. Questions that have been debated for a long time are whether or not the brain and other tissues of the head are in fact developed in a segmental fashion and, if so, which structures are within each segment. Although neuromeres have yet to be identified in the developing spinal cord, the spinal cord in adult vertebrates clearly is a segmented structure. Each segment of the spinal cord has dorsal and ventral pairs of spinal nerves that innervate each successive segment of the body, but the segmental organization of the brain has not been as easily understood.

Recent advances from studies of the embryology of the head, using modern transplant and marking techniques, have led to a new perspective on the development of the head and brain in vertebrates through an understanding of the roles of two ectodermal (outer body layer) derivatives, the **neural crest** and **neurogenic placodes**, and also of the role of different components of the mesoderm (middle body layer) in this process. In addition to the process of segmentation of neuromeres within the neural tube itself, at least some of these

other tissues interact in a segmental fashion during the development of the brain and sensory organs. To approach this topic, we first need to review briefly some of the components of the skeleton of the head. We then need to consider the relationship of these skeletal components to the striated, somatic musculature of the head and the embryological derivation of these muscles in relation to the somatic and visceral muscles of the body. We also need to consider the embryological derivation of the various ganglia for the nonvisual sensory cranial nerve components. The sum of these findings allows us to all but discard the “special” categories for cranial nerve components and to achieve a new appreciation of cranial nerve organization. Although some cranial nerves have multiple components and appear somewhat complicated at first, the new perspective that recently has been gained greatly simplifies and illuminates their organization.

Head Skeleton

The skeleton of the head in hagfishes, lampreys, and cartilaginous fishes (chondrichthyans) contains two components: the **chondrocranium**, which encloses the special sense organs and forms part of the braincase, and the **splanchnocranium** (or **visceral arches**), which supports and moves the gills and contributes to the jaws, hyoid, and throat regions. These components are shown in Figure 9-1(A) as they occurred in early jawed vertebrates. In bony fishes and sarcopterygians, including tetrapods, a third component is present: the **dermatocranium** (or **dermal bones**), which contributes to the braincase and the jaws. The chondrocranium and splanchnocranium are almost entirely of neural crest origin, as we will discuss further below, while the dermatocranium arises from a combination of neural crest and mesodermal sources. In vertebrates that have gills, the first step in the development of the gills is the formation of a paired series of pouches that arise as evaginations (out-growths) from the pharynx in the throat region and lie between the visceral arches [Fig. 9-1(A)].

The first visceral arch, which is the **mandibular arch** in jawed vertebrates, lies rostral to the first pharyngeal pouch (which is reduced to the small **spiracle** or lost altogether due to space constraints), and the second visceral arch, or **hyoid arch**, lies between the first and second pharyngeal pouches. Most jawed fishes [Fig. 9-1(A,B)] and tetrapods have five additional visceral arches, which are called the first through the fifth **branchial arches**. The term branchial refers to the gills. In cartilaginous fishes, the mandibular arch consists of a dorsal palatoquadrate cartilage and a lower mandibular cartilage that form the upper and lower jaws, respectively. In bony fishes [Fig. 9-1(B)] and tetrapods [Fig. 9-1(C,D)], the dermatocranium contributes substantially to the bony part of the jaws; remnants of the palatoquadrate and mandibular cartilages are retained in bony fishes, however. In mammals [Fig. 9-1(C)], the posterior parts of the mandibular and palatoquadrate cartilages—the articular and quadrate, respectively—are incorporated into the middle ear as the malleus and incus, respectively. In nonmammalian tetrapods [Fig. 9-1(D)], the cartilaginous articulation of the jaws is derived from the articular and quadrate components of the mandibular arch.

The dorsal part of the hyoid arch, called the hyomandibula [Fig. 9-1(A)], suspends the palatoquadrate cartilage in bony

fishes, and its ventral part extends ventrally into the mouth and pharynx. In tetrapods, the hyomandibula forms one of the auditory ossicles—known as the columella in extant reptiles and birds and as the stapes in mammals—while most of the branchial arches are incorporated into the various cartilages of the throat (hyoid, thyroid, cricoid, etc.). The muscles associated with the whole series of visceral arches are referred to as **branchiomic muscles**.

The Striated Musculature of the Head

One of the major breakthroughs in understanding the development of the head and central nervous system was the recent identification of the embryonic source of all of the striated muscles in the head. To appreciate the situation in the head, we first need to understand the situation in the body. In the body, the mesoderm arises during gastrulation (see Chapter 3) and forms the middle layer. The mesoderm forms the notochord in the midline. The mesoderm that lies lateral to the notochord has three major divisions [Fig. 9-2(A)]. The most dorsal division is called **epimere**, or **paraxial mesoderm**. It forms a segmental, rostrocaudal series of masses called **somites**, which give rise to the dermis of the skin, the striated muscles of the body wall, including the limb muscles, and the vertebral column and occipital region of the skull. The second division of the mesoderm is relatively small. It is called the mesomere, or intermediate mesoderm, and it gives rise to the nephric ridge and the genital, or gonadal, ridge, which contribute to the kidneys and gonads, respectively. The third and most ventral division of the mesoderm is called the **hypomere**, or **lateral plate mesoderm**. Part of the hypomere contributes to the somatic, striated muscles of the abdominal wall, but its inner layer gives rise to the nonstriated, visceral muscles and connective tissues of the gut in conjunction with the endodermal lining of the gut.

The branchiomic muscles associated with the jaws, hyoid arch, and gills (branchial) or throat cartilages within the head were long thought to be derived from a rostral extension of the hypomere (the lateral plate mesoderm) and therefore of visceral origin. The cranial nerves supplying them were therefore classified as visceral motor (efferent) nerves. Only the extraocular muscles of the eye and the muscles of the tongue were thought to be somatic muscles, that is, derived from the embryonic epimere (paraxial mesoderm) in the head. The fact that the supposedly visceral, branchiomic muscles are striated in their histology and under voluntary control, like the extraocular eye muscles and the tongue, was an unresolved problem and was dealt with by classifying their cranial nerve components as “special.” The belief that the branchiomic muscles are visceral in embryonic origin has been contradicted by contemporary embryology.

Interspecies transplantation studies and cell lineage tracing studies have allowed a reexamination of the fate of the mesoderm within the head, revealing a rather different story. In the developing head, the epimere (paraxial mesoderm) forms a rostrocaudal, segmented series of slightly elevated bulges. In the caudal part of the head, these bulges form separate masses just as in the body and are likewise called somites. In the more rostral part of the epimeric column, the bulges are not entirely separate and so are called **somitomeres**.

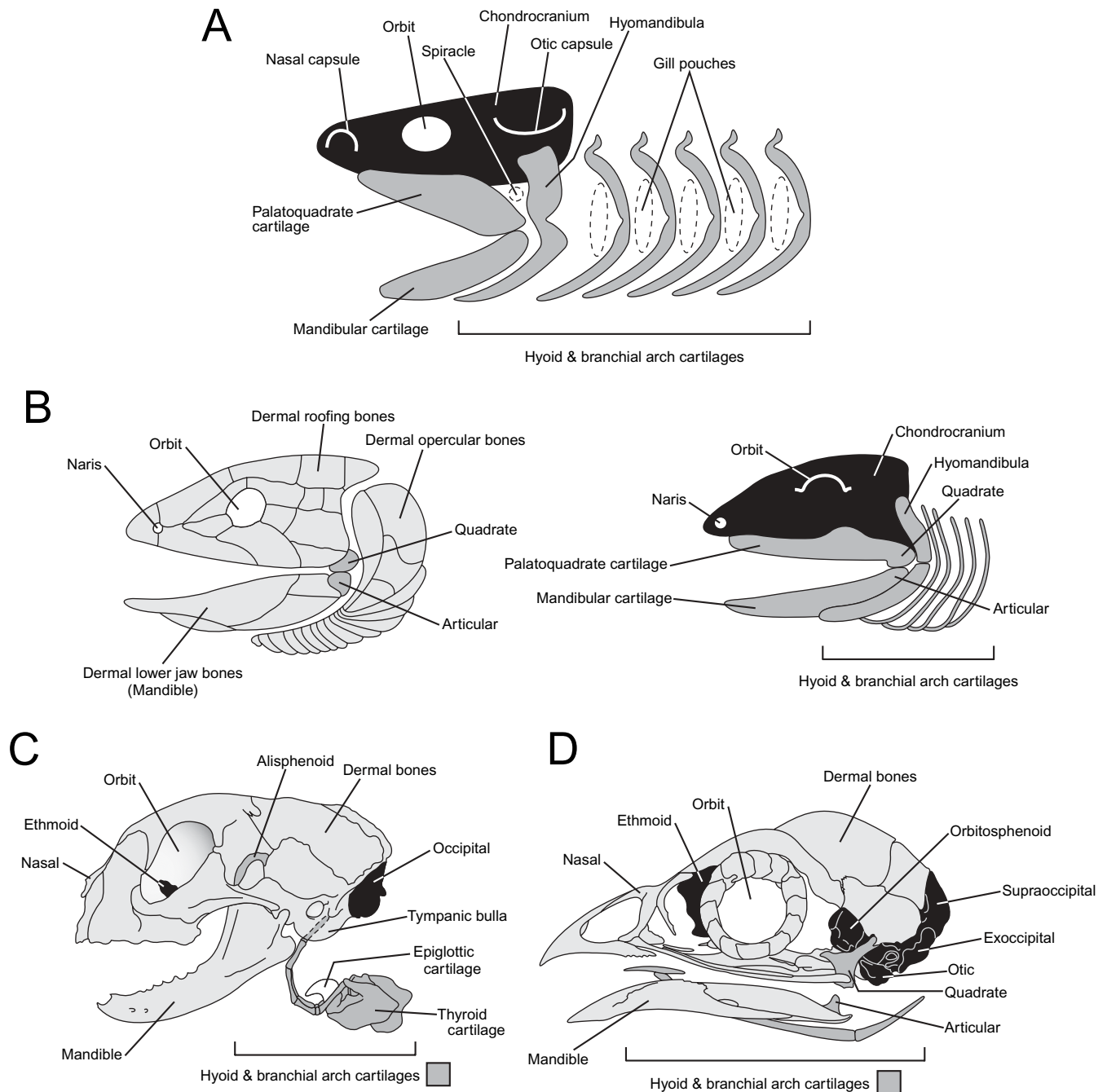


FIGURE 9-1. Elements of the vertebrate skull. **A:** Chondrocranium (in black) and splanchnocranium (in medium gray) of the skull of an early jawed vertebrate. The splanchnocranium comprises the palatoquadrate and mandibular cartilages of the first visceral arch, the hyoid (second visceral) arch, and five branchial arches. The upper part of the hyoid arch is the hyomandibular cartilage. **B:** Skull of a generalized bony fish. Dermatocranium (in light gray) shown on the left along with articular and quadrate parts of splanchnocranium, which would overlie the chondrocranial and splanchnocranial elements shown on the right. The articular and quadrate form the jaw joint. **C:** Skull of the domestic cat. The dermatocranium comprises much of the skull and the mandible, and part of the splanchnocranium—the alisphenoid bone—is incorporated into the skull caudal to the orbit. Visible chondrocranial elements are the occipital and ethmoid bones. The articular and quadrate are not visible, since they have been incorporated into the middle ear as the malleus and incus, respectively, as has the hyomandibular as the stapes. **D:** Skull of a bird (a gosling, *Anser ferus*). Visible chondrocranial elements include the ethmoid, orbitosphenoid, occipital (supraoccipital and exoccipital), and otic bones. The articular and quadrate are external to the ear, but the hyomandibular has been incorporated into the middle ear as the columella. Based on figures from Liem et al. (2001) and used with permission of Thomson Learning Global Permissions Group.

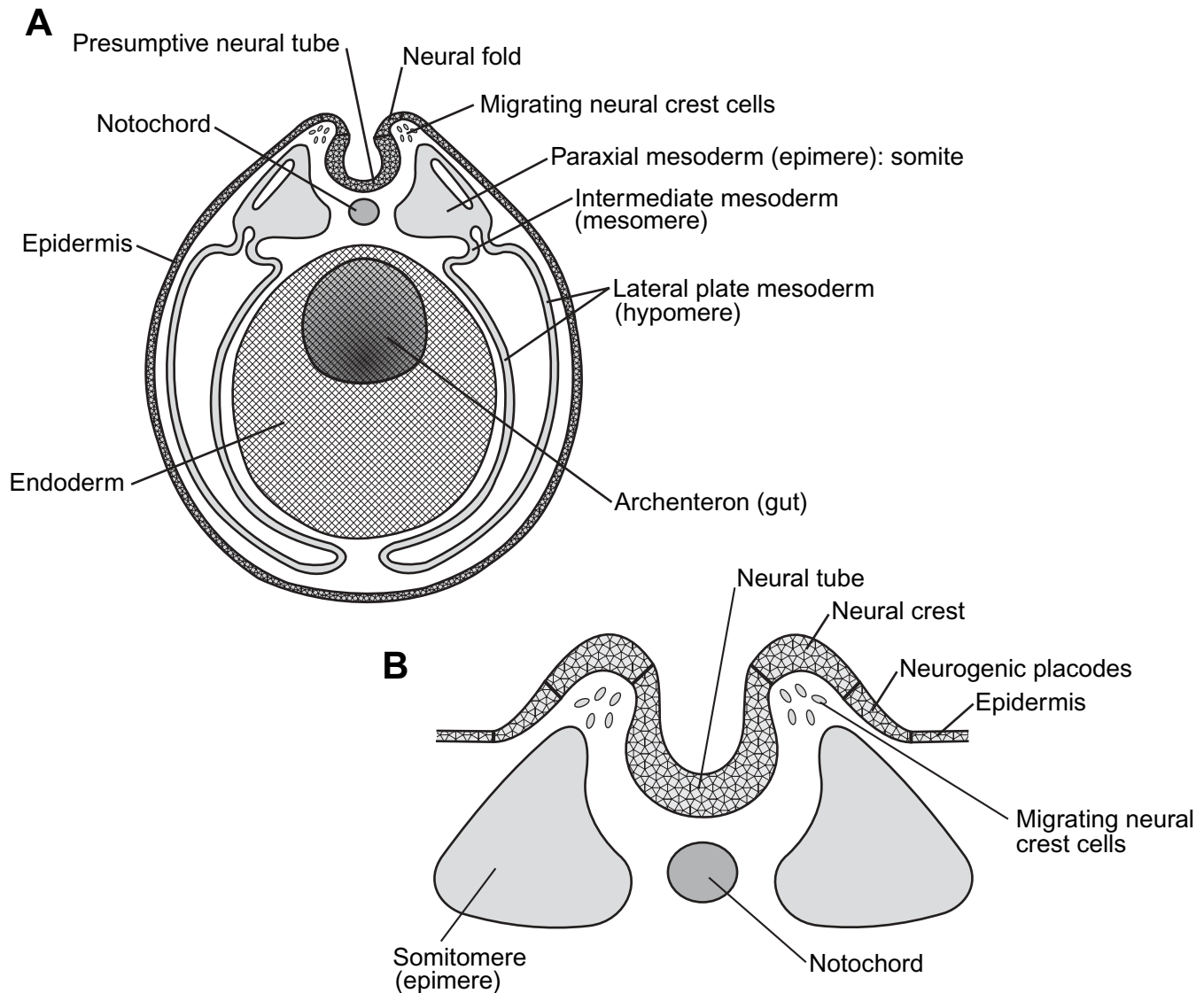


FIGURE 9-2. A: Schematic transverse section through a vertebrate embryo to show the organization of the developing neural tube and neural crest and of the mesoderm in the body, which comprises epimere, mesomere, and hypomere. B: Schematic drawing of an enlargement of the upper part of the drawing shown in A but in the head region to show the presence neurogenic placodes lateral to the neural crest and of somitomeres, which are derived from epimere and give rise to all of the voluntary, striated muscles of the head. Based on figures from Liem et al. (2001) and used with permission of Thomson Learning Global Permissions Group.

[Figs. 9-2(B) and 9-3]. The mesomere (intermediate mesoderm) does not extend into the head region at all, and there is only a very small component of hypomere (lateral plate mesoderm) in the head, which contains precursors of cells that make a minor contribution to some of the throat cartilages and neighboring bone. The hypomere does not contribute to somite or somitomere formation, so the latter tissues have no component that is developmentally visceral.

Thus, the column of somitomeres and somites are the only division of the mesoderm in the head that gives rise to muscle. They give rise to all of the striated muscles of the head—extraocular, branchiomic, and tongue muscles—(Fig. 9-3),

just as the somites of the epimere in the body give rise to the striated muscles of the trunk and limbs. Thus, the voluntary striated muscles in the head, which are innervated by cranial motor nerves, are all somatic muscles, and their motor nerves are all somatic motor nerves. The cranial nerve components that innervate the branchiomic muscles, classified as “special visceral efferent,” are neither special nor visceral. The “efferent” part of the traditional classification alone stands as correct. These cranial nerve components are simply somatic efferent. Some argue that they should still be distinguished from the components that innervate the eye and tongue muscles due to the relatively migrated position of their nuclei within the brain—

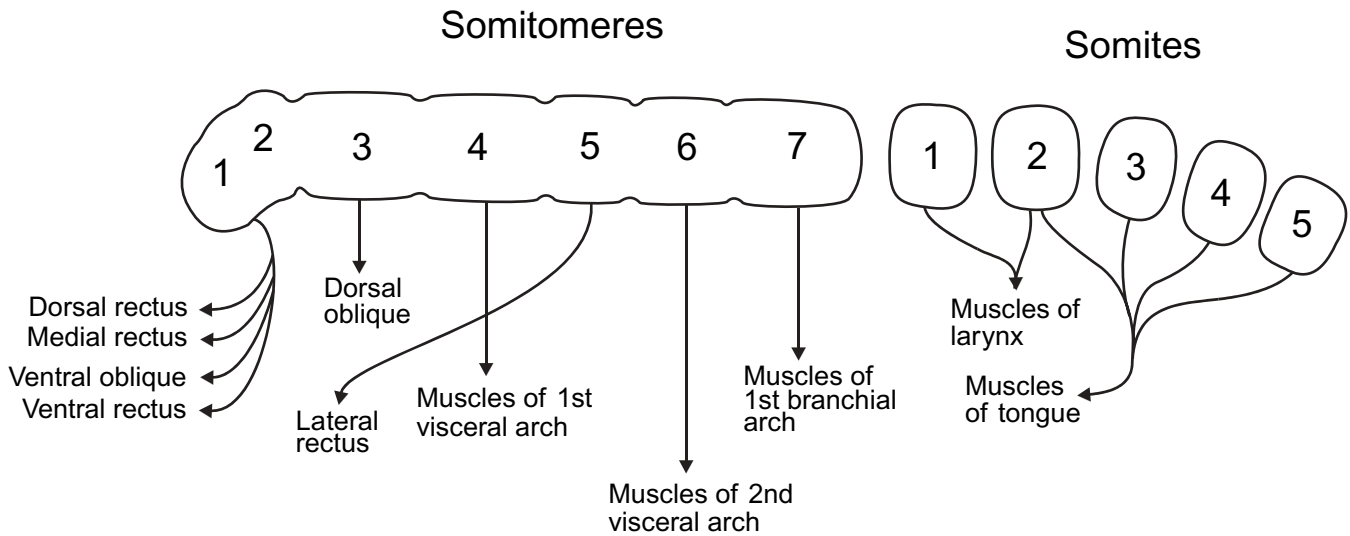


FIGURE 9-3. Schematic drawing in the parasagittal plane of the epimeric mesoderm in the head and the muscles that each part of it gives rise to. Rostral is toward the left. Adapted from Noden (1991) and used with permission of S. Karger AG, Basel.

stem, as we will discuss below. However, simple somatotopy (the same medial-to-lateral organization of nuclei and the muscles they innervate) may account for this difference, and the migration in some vertebrates of at least one of the nuclei that innervate the extraocular muscles, also discussed below, weakens this position. In the final analysis, these cranial nerve components might best be regarded simply as branchiomic somatic efferent components if one wishes to make any distinction at all.

Neural Crest and Placodes

Studies of the movement and fate of neural crest cells and other populations of ectodermally derived cells have also revealed new findings about the development of the brain and head. Neural crest cells arise within the neural fold tissue lateral to the neural tube in both the body and the head (Figs. 9-2 and 9-4), as discussed in Chapter 3. In the head, these cells are segmentally specified at their point of origin by the pattern of expression of homeobox-containing regulatory genes, and they carry their segmental identity as they migrate ventrolaterally between the paraxial mesoderm and the surface ectoderm. The neural crest gives rise to many structures throughout the body, including nerves and sensory ganglia in the trunk, chromaffin cells, which secrete adrenalin in the medulla of the adrenal gland, all pigment cells, and the Schwann cells that supply the myelin sheathing around peripheral nerves. In the head, neural crest cells migrate between the pharyngeal pouches. These cells form the cartilage of the branchial arches and the smooth muscle of the aortic arches. Within the rest of the head, the neural crest gives rise to the anterior part of the neurocranium and to the meninges, the connective tissue layers that cover the brain. It also gives rise to a number of the cranial nerves and their sensory ganglia.

Parts of the surface ectoderm also contribute to the formation of cranial nerves and sensory ganglia. Patches of

neurogenic tissue form within the ectoderm. These patches are called neurogenic placodes (Fig. 9-5), and they give rise to additional components of the nervous system. Neural crest cells migrate beneath the placodes, and the placodes then begin to produce neuroblasts (nerve cell precursors). A dorsolateral series, a ventrolateral series, and additional unclassified sets of placodes form the sensory receptors and ganglia of some of the cranial nerves. Although neural crest occurs throughout the head and body, placodes are present only in the head.

All of the sensory bipolar neurons for the peripherally lying ganglia of the nonvisual cranial nerve components are thus derived from the two tissues: neural crest and neurogenic placodes. In the body, all of the bipolar sensory neurons are derived from just the neural crest, whereas placodes additionally contribute in the head. The designation of “special” for some of the sensory cranial nerve components does not, however, coincide one-to-one with the additional or sole contribution of bipolar neurons from placodes, nor are placodes different in any “special” way from other regions of neurogenic ectoderm. As discussed in Chapter 3, during embryological development, all ectoderm initially has the potential to give rise to neurons, but this propensity is suppressed by bone morphogenetic proteins (BMPs). The expression of chordin and other proteins from the underlying mesoderm in the dorsal midline blocks the BMP receptor sites and allows the ectoderm to achieve a neural fate. Thus, while the neurons derived from the neural tube, neural crest and neurogenic placodes differ in their degree of exposure to the mostly suppressed BMPs, at a more fundamental level, they are all just neurons derived from ectoderm. In fact, in fruit flies and other arthropods, the sensory neurons that project into the central nervous system are simply derived from surface ectoderm cells at various locations over the body surface. Rather than originating near the neural tube like neural crest and placodes, they simply originate locally and then give rise to an axon that grows toward and then into the brain or nerve cord.

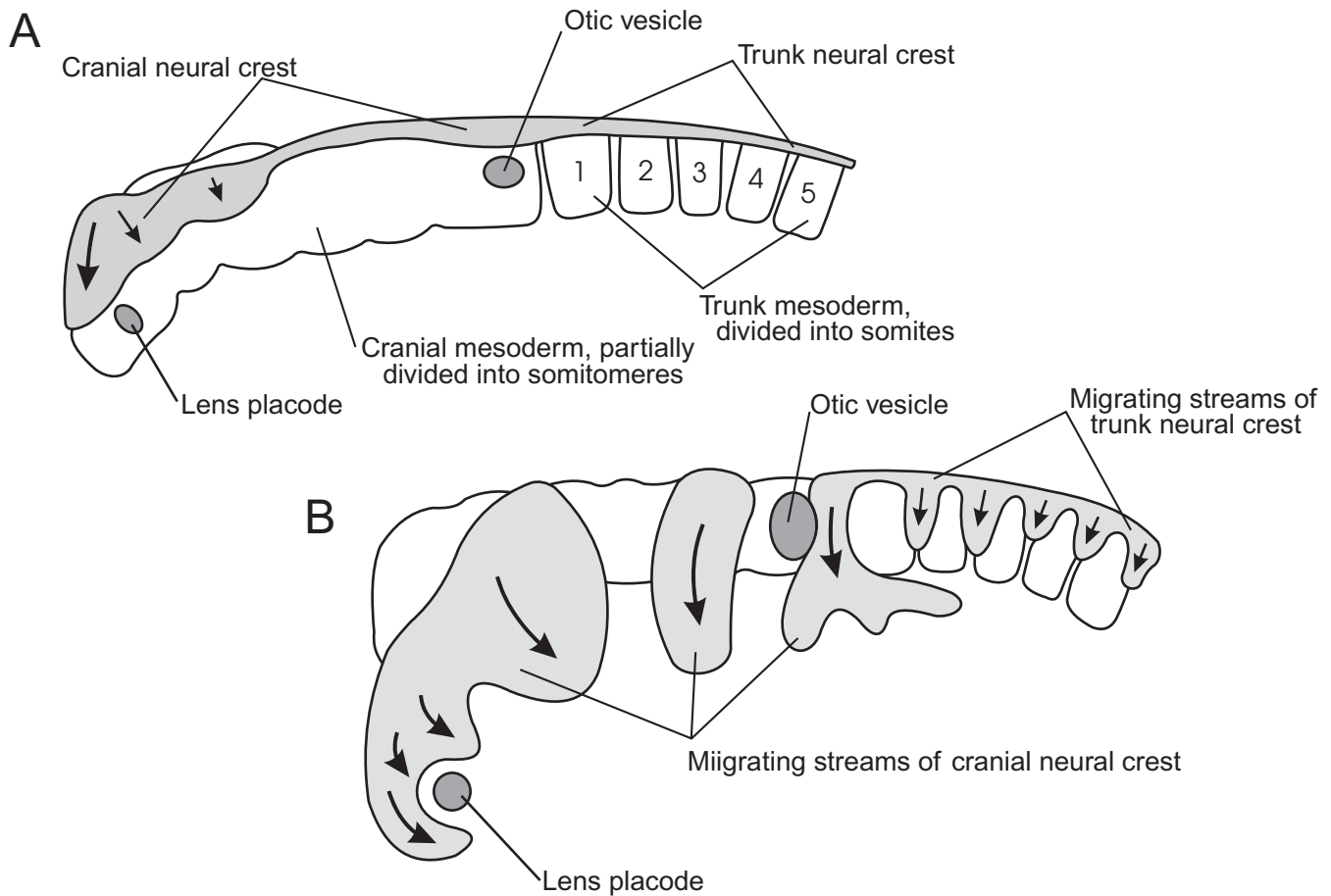


FIGURE 9-4. Schematic drawings of parasagittal sections through the developing rostrrodorsal part of a vertebrate embryo at earlier (A) and later (B) stages, showing the somitomeres and somites and with neural crest tissue migrating ventrolaterally over them, as indicated by arrows. Rostral is toward the left. Adapted from Noden (1991) and used with permission of S. Karger AG, Basel.

In vertebrates, the bipolar neurons of the cranial nerve components for the telencephalic-related olfactory senses (olfactory and vomeronasal) arise from the rostrally lying nasal placode (Fig. 9-5). The GnRH (gonadotropin-releasing hormone)-positive neurons of the terminal nerve arise not from the olfactory placode as previously thought but rather from neural crest. The bipolar neurons for the modality of taste arise from three placodes of the **ventrolateral**, or **epibranchial, series**—hyoid (for cranial nerve VII), glossopharyngeal (for cranial nerve IX), and vagal (for cranial nerve X)—and contribute to one of the two ganglia that each of these nerves has. The bipolar neurons for the hearing and vestibular senses arise from the octaval placode, and, where present, the lateral line bipolar neurons arise from a series of placodes in the same region. These placodes are derived from the **dorsolateral series** of placodes, with only the octaval placode present in land vertebrates. Thus, cranial nerve components that have been traditionally classified as “special visceral afferent” (SVA) arise from placodes, as do those classified as “special somatic afferent” (SSA) and those for the olfactory senses of the telencephalon.

At this juncture, one might think that “special” is actually a legitimate distinction that could be applied to placodally

derived sensory neurons, but the trigeminal ganglion, which contains sensory neurons for the “general” senses of touch, position, pain, and temperature, negates that possibility. The latter senses are mainly carried to the brain via the trigeminal nerve (V) and, at least in mammals, also for small areas of the skin near and within the ear via three more caudal cranial nerves—VII, IX, and X. The latter three nerves each have two peripheral ganglia—one for taste, as described above, and a second for the touch-related senses, which is derived from neural crest. The large population of neurons within the single ganglion for the trigeminal nerve are, however, derived from both placodes—the **trigeminal** and **profundus placodes**—and from neural crest. These sensory neurons do not convey any of the “special” senses such as taste or hearing into the trigeminal system; they convey only senses served by neural crest-derived neurons alone in the body and are classified as “general.” Further, small or even larger contributions of neural crest to other sensory ganglia derived from placodes have not been ruled out.

The commonality that unites all cranial nerve components (except the visual) for sensory innervation in the head is thus the derivation of their bipolar neurons from placodes and/or

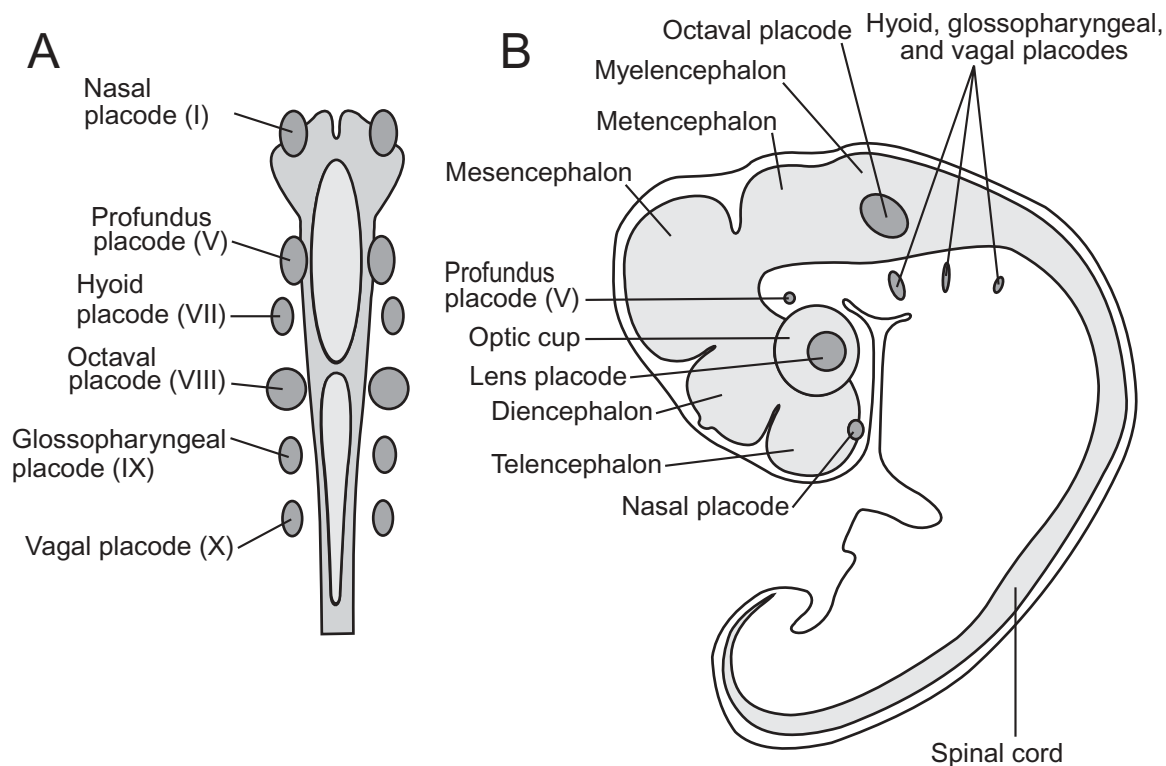


FIGURE 9-5. A: Schematic dorsal view of the developing brain (light gray), neural crest (medium gray), and the rostrocaudal sets of neurogenic placodes in an amniote embryo. Dorsal is toward the top. B: Schematic drawing of a parasagittal section through an amniote (chick) embryo, showing the central nervous system (lighter gray) and the lens placode and the sets of neurogenic placodes (darker gray). Rostral is toward the left with caudal proceeding in the clockwise direction. Adapted from Liem et al. (2001) and used with permission of Thomson Learning Global Permissions Group.

neural crest, i.e., the surface ectoderm dorsolateral to the neural tube. This includes the senses previously classified as “special” and as “general,” for which this distinction now collapses. In our discussion of these sensory cranial nerves, we will therefore distinguish those derived mainly from various placodes but only classify them as to whether they are somatic or visceral in their receptor innervation. We will note the traditional classification only in the context of historical interest and because of its continued prevalence in some contemporary literature.

Segmentation of the Head

The head in vertebrates differs from the rest of the body in two significant ways: the hypomere (lateral plate mesoderm) is present but makes only modest contributions to cartilage and bone rather than giving rise to muscle, and neurogenic placodes are present. The contributions of placodes and neural crest result in the formation of the paired, nonvisual sense organs and the anterior part of the neurocranium, that is, the rostral part of the head, which is thus new in vertebrates. This formation of a new part of the head due to the presence of placodes and neural crest and its implications for the origin of vertebrates were recognized by Carl Gans and R. Glenn Northcutt in 1985.

Like the body, the head is segmented, that is, composed of repeating units. These units may or may not be serially homologous (iterative) to the segments of the spinal cord, spinal column, and body wall, but they exhibit organizational similarities. The segmental units include the expression patterns of regulatory genes, morphological neural units (neuromeres), populations of motor neurons for cranial nerves, morphological epimeric (paraxial mesodermal) elements (which form the somites and somitomeres of the head region), and streams of segmentally specified neural crest cells. Some of the cranial nerves are organized like segmented spinal nerves. Other cranial nerves, including those derived from placodes, are for the most part unique to the head in terms of their modalities.

In creating a model of head segmentation for vertebrates, a simple one to one correspondence among specific neuromeres, somitomeres, and visceral arches has not yet been delineated. The series of rhombomeres that form the hindbrain is highly conserved among vertebrates, but variation occurs in the location of some of the cranial nerve motor nuclei (Fig. 9-6). The series of somitomeres is also highly conserved, but a precise, topographic registration of somitomeres with neuromeres has yet to be confirmed.

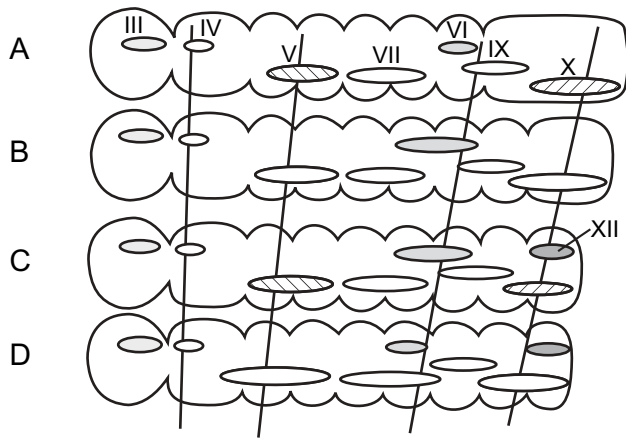


FIGURE 9-6. Schematic drawings to show the relationships between neuromeres and cranial nerve motor nuclei in a variety of vertebrate groups. Shadings and vertically running lines are used to facilitate comparisons of the relative positions and extent of the cranial nerve nuclei, which are indicated by their Roman numerals. A: Elasmobranch. B: Teleost fish. C: Nonmammalian amniote. D: Mammal. Rostral is toward the left. Adapted from Gilland and Baker (1993).

THEORETICAL HEAD SEGMENTS

A head segment (or the concept of a head segment) encompasses elements of each of the segmentally organized tissues in the vertebrate head. Thus, a model head segment would contain a rostrocaudally defined portion of the neuromeres, at least some of the cranial nerve neurons, somitomeres, neural crest, visceral arches, and related tissues. Placodes may be influenced by segmentally specified neural crest but may not in themselves be segmentally organized. Because the rostrocaudal alignment of the various segmental tissues varies among different groups of vertebrates, the definitive head segment cannot yet be identified. Nonetheless, we can examine the organization of the cranial nerves with a theoretical model of head segments.

The overall organizational pattern that emerges reveals the presence of up to four separately derived nerves—**dorsal**, **ventral**, **dorsolateral**, and **ventrolateral**—for each side of each head segment. All four nerves are not present in all head segments, but we have illustrated all four schematically in Figure 9-7 to make the segmental organizational pattern clear.

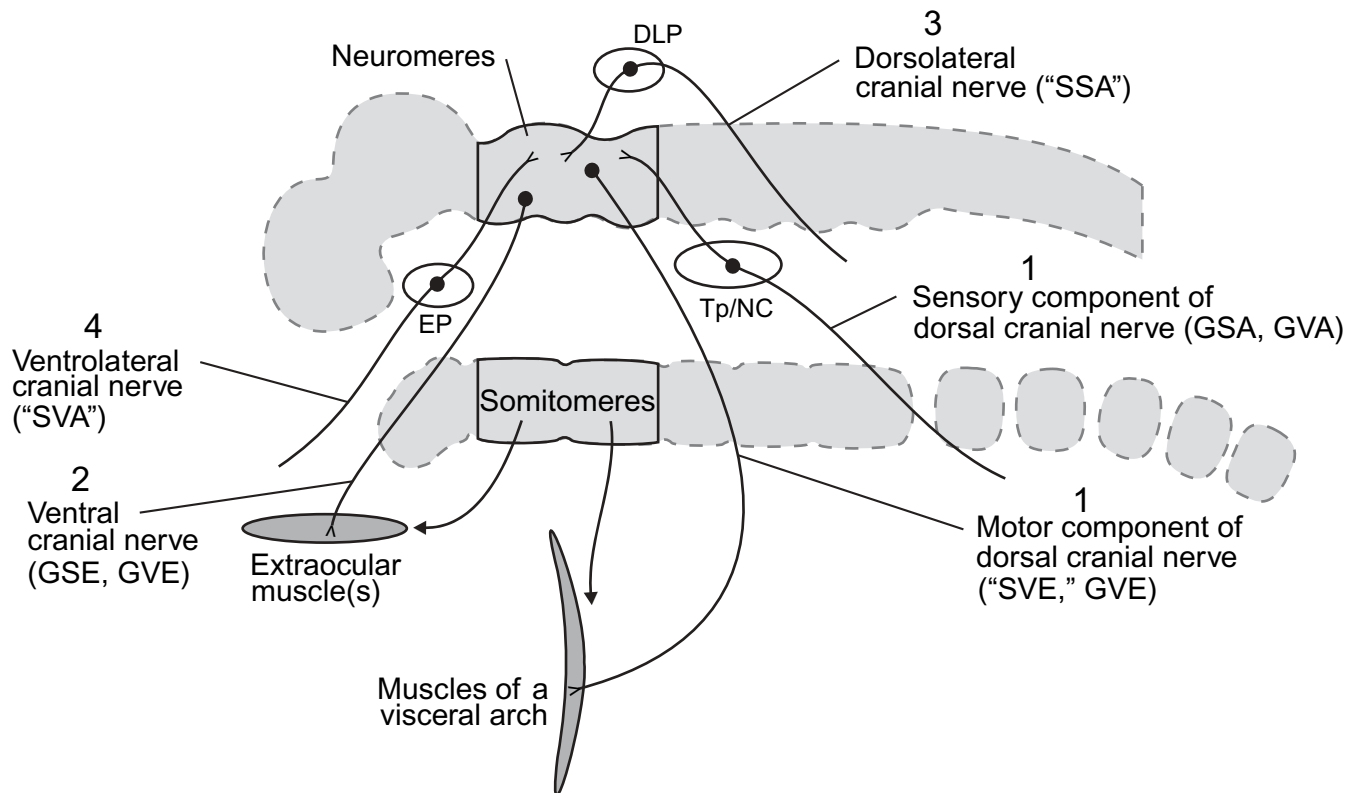


FIGURE 9-7. Schematic drawing of a complete theoretical head segment to show the organizational plan of the cranial nerves. Such a complete segment does not exist in reality. The segment shown here is a composite of elements from the second and third head segment. It includes a 1) dorsal nerve with both sensory and motor components, 2) ventral nerve that is purely motor, 3) dorsolateral sensory nerve, and 4) ventrolateral sensory nerve. It includes a pair of somitomeres that give rise to one or more of the muscles of the eye (or tongue) and to some of the branchiomeric muscles of the visceral arches. Rostral is toward the left. Note that the general visceral, parasympathetic components are not separately included in this figure. The axons of preganglionic parasympathetic neurons exit the brain either via ventral (VII) or dorsal (VII_D, IX_D, and X_D) nerves. See Figure 9-8 and text for abbreviations.

Figure 9-7 shows a complete theoretical head segment, derived from a composite of elements from both the second and third head segments. It includes a pair of somitomeres, the more rostral of which gives rise to one or more of the muscles of the eye or to the muscles of the tongue. The more caudal somitomere of each pair (except the first) gives rise to branchiomeric muscles.

The dorsal nerve for the segment contains both sensory and motor components. Sensory axons ("GSA") derived from placodes and/or neural crest project into the sensory nuclei in the alar plate of the neural tube. This sensory component corresponds to that seen in the dorsal root axons of the spinal cord. Additionally, the dorsal nerve contains motor fibers, unlike the dorsal roots of the spinal cord. These fibers ("SVE") innervate the branchiomeric muscles(s) that are derived from the more caudal of the two somitomeres. The ventral nerve for a given model segment is derived from cells in the ventral part of the neural tube. This nerve is the somatic motor nerve ("GSE") for the muscle(s) derived from the more rostral of the two somitomeres. This arrangement appears to correspond to that seen in the spinal cord, with the ventral, nerve carrying somatic motor fibers. Unlike the situation in the spinal cord, parasympathetic ("GVE") components exit the brainstem either via ventral or dorsal segmental nerves.

The sensory ganglion cells of two additional nerves in the segment are derived mainly or fully from placodes. As discussed above, additional research is needed to clarify the origin from placodes and/or neural crest of a number of cranial nerve sensory ganglia. The dorsolateral nerve of a model segment is known to be derived from the dorsolateral series of placodes. In the third head segment, multiple dorsolateral nerves are in fact present in aquatic vertebrates, and the placodes give rise to the receptors and sensory ganglion cells of the auditory, vestibular, and lateral line systems. Only one of these nerves is included in the model segment shown in Figure 9-7. A ventrolateral nerve for the segment can be modeled, subject to further research findings, as deriving from the ventrolateral (or epibranchial) series of placodes, which give rise to the sensory ganglion cells for the sense of taste.

This head segment model does not apply readily to the forebrain. The most rostral cranial nerves are sensory and are associated with the forebrain, which lies rostral to the first model head segment. The telencephalic cranial nerves are derived from placodes, but these placodes are not part of the ventrolateral or dorsolateral series, nor are dorsal or ventral nerves present in the forebrain. An additional difference is that the forebrain has two unique nerves, derived from evaginations of the brain itself: the optic and the epiphyseal nerves.

From the above description, it should be apparent that there is a general scheme of organization of the cranial nerves. For a model head segment (Fig. 9-7), up to four separate cranial nerves are present: (1) a dorsal nerve, with a motor component derived from the neural tube that innervates branchiomeric muscles and one or two components derived from placodes and/or neural crest cells that are sensory; (2) a ventral nerve derived from the neural tube that is motor; (3) a sensory nerve derived from dorsolateral placodes; and (4) a sensory nerve derived from ventrolateral placodes and/or neural crest. As discussed above, the modeled embryological derivation of some of these components may be modified as further data

become available. Variation occurs in the presence of some of the nerves among different model head segments, but the differential patterns of organization of the cranial nerves in each segment can be understood in terms of the basic theme. The model segments of the head thus resemble the actual segments of the spinal cord in having dorsal and ventral nerves, but model head segments additionally have motor components of dorsal nerves and dorsolateral and ventrolateral nerves contributed by placodes and/or neural crest.

SEGMENTAL ORGANIZATION OF THE INDIVIDUAL CRANIAL NERVES

We will now examine the organization of cranial nerves in the forebrain and in a rostrocaudal series of head segments. These segments only represent a hypothetical, generalized vertebrate scheme, since a simple one to one correspondence of neuromeres, somitomeres, and other segmental tissues of the head has not been defined across all vertebrate groups. With the overall scheme of a model head segment that was presented in Figure 9-7 in mind, the organization of the various, individual cranial nerves can be understood. Figure 9-8 is a comprehensive diagram that illustrates the cranial nerves of the forebrain and the successive head segments along with the neuromeres, somitomeres, and currently hypothesized contributions from neural crest and placodes. The alignment of the head segments with the neuromeres and somitomeres in Figure 9-8 is based only on our generalized, theoretical model of vertebrate head segmentation, as discussed above.

Table 9-2 summarizes the segmental organization of the head and the cranial nerves. The original terminology used for the cranial nerves has been modified only slightly for the new scheme. As we will discuss below, three of the traditionally recognized 12 cranial nerves actually comprise two separate nerves each. The facial, glossopharyngeal, and vagus nerves each contain the components of a dorsal, segmental, cranial nerve and a ventrolateral cranial nerve derived from the series of epibranchial placodes. In each of these cases, we refer to the former as a separate nerve from the latter. Thus, for example, we refer to the "dorsal facial (VII_D) nerve" and the "ventrolateral facial (VII_V) nerve" rather than to just the "facial (VII) nerve." In cases where only one of the segmental nerves (i.e., dorsal, ventral, ventrolateral, or dorsolateral) is contained in a designated nerve or where a placodal component of a nerve remains undesignated, we do not use an adjective to modify the original name of the nerve. For example, although the trigeminal nerve is a dorsal cranial nerve that also has a placodal component, it is not subdivided here into dorsal and either ventrolateral or dorsolateral components. We refer to it simply as the trigeminal (V) nerve.

The model presented in Figure 9-8 is a neuromere-somitomere model of the development of the head and the cranial nerves. It is based on several publications, including those of Northcutt (1990), Noden (1991), and Liem et al. (2001). This model may be subject to revision as new data continue to be obtained. For example, data and analyses published by Gilland and Baker (1992, 1993) and by Northcutt (1993) suggest a revised numbering system for the somitomeres such

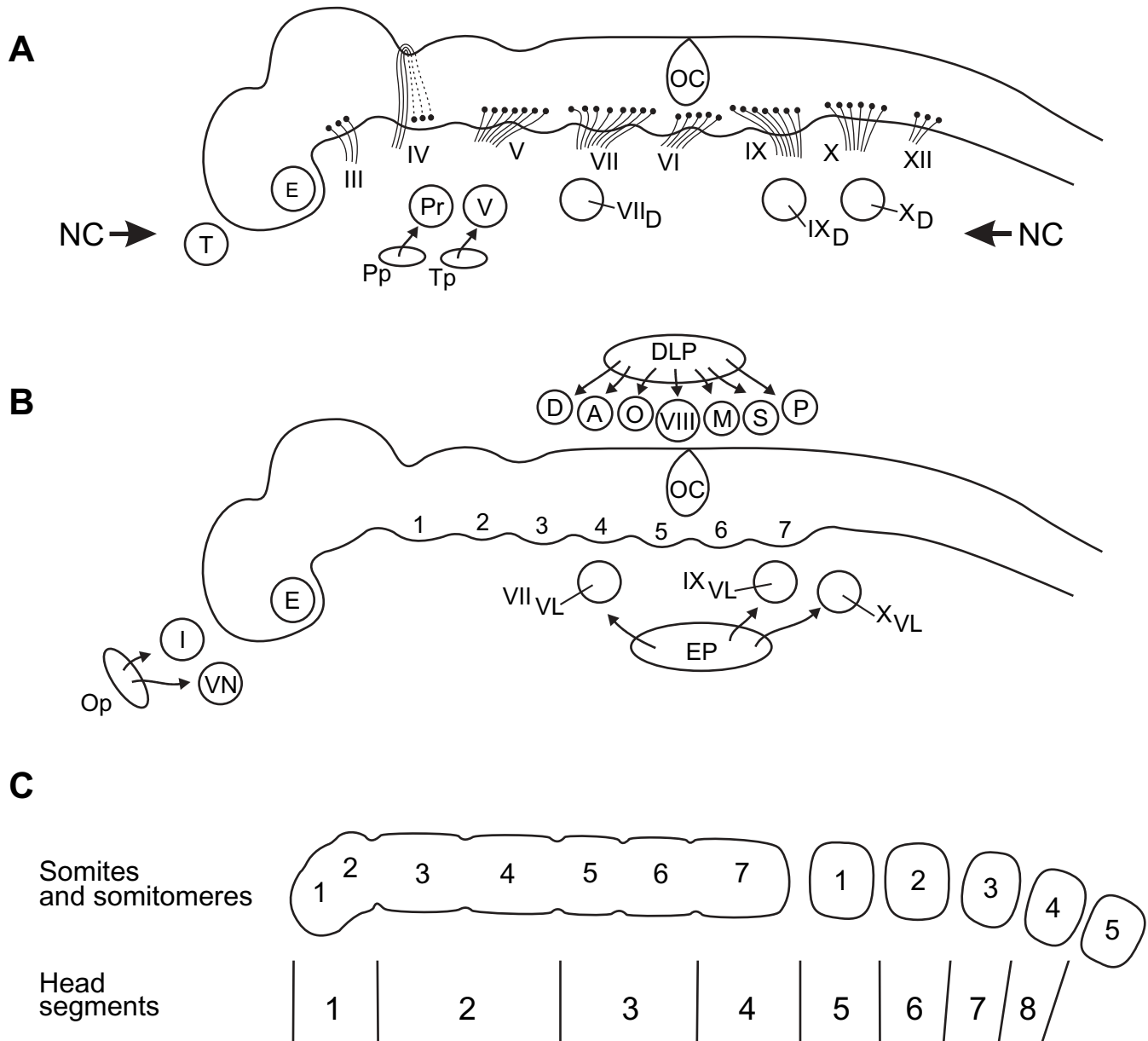


FIGURE 9-8. Schematic drawing of parasagittal sections through the neural tube (A and B) and the somitomeric mesoderm aligned with the model head segments (C). The derivation of cranial nerve cells and ganglia (T, V, VII_D, IX_D and X_D) from neural crest (NC with arrow), with contributions to V from the trigeminal (T_P) and profundus (P_P) placodes, and the location of their respective sensory ganglia peripheral to the neural tube are shown in A, as are the neuron cell bodies within the neural tube for most of the various motor cranial nerve components. The derivation of cranial nerve ganglia and nerves from the dorsolateral (DLP) and ventrolateral, epibranchial (EP) series of placodes and the rostral olfactory (O_R) placode are shown in B. The rhombomeres are indicated by Arabic numerals 1–7 in B. The somitomeres (Arabic numerals 1–7) and rostral series of somites (Arabic numerals 1–5) along with model head segments (Arabic numerals 1–8) are shown in C in vertical alignment with the neural tube. Cranial nerve components are identified by their Roman numerals or by the abbreviations: A, anteroventral lateral line; D, anterodorsal lateral line; M, middle lateral line; O, otic lateral line; P, posterior lateral line; Pr, profundus; S, supratemporal lateral line; T, terminal; and VN, vomeronasal. Other abbreviations: OC, otic capsule; E, eye (which lies within the forebrain). Rostral is toward the left and dorsal toward the top. Adapted from Noden (1991) and used with permission of S. Karger AG, Basel.

TABLE 9-2. Head Segmentation and Cranial Nerve Organization

Head Segment	Origin	Visceral Arch	Branchial Arch	Neural Tube-Derived	Neural Crest-Derived	Ventral Cranial Nerve	Dorsolateral Cranial Nerve	Forebrain Placodal or Ventrolateral Cranial Nerve
				II, Epiphyseal	T			I, VN
1	Somitomeres 1, 2				Profundus	III	LL _{AD}	
2	3, 4	1		Motor V	GSA V	IV	LL _{AV}	
3	5, 6	2		Motor VII _D	GSA VII _D	VI	Otic, VIII	VII _{VL}
4	7	3	1	Motor IX _D	GSA & GVA IX _D		LL _M	IX _{VL}
5	Somites 1	4	2	Motor X _D	GSA & GVA X _D	XII	LL _{ST} , LL _P	X _{VL}
6–8	2–4	5–7	3–5	Motor X _D		Occipital		X _{VL}

that somitomeres 1–3 as shown here would be the prechordal plate (mesoderm that is located rostral to the rostral end of the notochord), and seven somitomeres would then be recognized in the region presently considered to be somitomeres 4–7. Still other designations of the somitomeres have also been proposed. The rostrocaudal order of neuromere-somitomere model units remains relatively constant, however, and that order is the key point to keep in mind in analyzing the organization of the cranial nerves.

The Forebrain

The first several cranial nerves are associated with the forebrain, which lies rostral to the first model head segment. The most rostral cranial nerve is the **terminal nerve**, the cell bodies of which contain GnRH and are derived from the cranial neural crest [Fig. 9-8(A)]. The dendrites of terminal nerve neurons are distributed over the nasal septum, and the axons project to various sites in the forebrain. This nerve may play a role in reproductive behaviors.

Cranial nerve I, the **olfactory nerve**, is derived from the **olfactory placode** [Fig. 9-8(B)]. This nerve carries olfactory information into the olfactory bulb at the rostral tip of the telencephalon, which in turn projects to the olfactory cortex within the telencephalon proper. The **vomerolateral nerve** is another cranial nerve that is present in some but not all vertebrates and is associated with the olfactory nerve and likewise derived from the olfactory placode. This nerve also plays a role in chemical detection. It projects, however, to an accessory olfactory bulb, which projects to areas of the telencephalon different from the main olfactory input areas. An additional placode present in this region (but not illustrated in Fig. 9-8) is the **adenohypophyseal placode**. It gives rise to GnRH-positive neurons that migrate to the hypothalamus. The olfactory organ and adenohypophysis arise from a single placode in lampreys, and a single rostral placode may thus be the pleiomorphic condition for vertebrates.

The **optic nerve**, cranial nerve II, arises from neurons in the retina, and the **epiphyseal nerve** (which in a number of groups of vertebrates has two divisions—a pineal nerve and a more rostral epiphyseal nerve) arises from neurons in the epiphysis. These cranial nerves should probably be considered as parts of the brain rather than as cranial nerves because, whereas other sensory nerves are derived from either neural crest and/or from placodes, the receptors and sensory ganglion cells of the retina in the eye and of the epiphyseal photoreceptor system are derived from evaginations of the neural tube. Only the lens of the eye, and probably the lens of the parietal eye where present, are derived from placodal tissue. We thus have classified these nerves as evaginated sensory afferents.

The telencephalon thus has three nerves. Of these, the olfactory and vomeronasal nerves are derived from a placode and are referred to as “**forebrain placodal**” nerves in Table 9-2. The third telencephalic cranial nerve, the terminal nerve, is derived from neural crest. The optic and epiphyseal nerves of the diencephalon are photosensory and are uniquely derived from the neural tube. Ventral, dorsolateral, and ventrolateral nerves, as present in the more caudal parts of the brain, are clearly absent in the forebrain.

The First Head Segment

The first head segment in our model contains the first two somitomeres [Fig. 9-8(C)]. The more rostral somitomere and possibly the more caudal one give rise to the extrinsic eye muscles (listed in Fig. 9-3) that are innervated by cranial nerve III, the **oculomotor nerve**. Thus, the oculomotor nerve [Fig. 9-8(A)] is the somatic motor nerve of the ventral part of the first head segment. The more caudal somitomere of this segment does not give rise to any branchiomeric muscle.

The profundus placode is currently not assigned to either the dorsolateral or ventrolateral series of placodes. It gives rise to most or all of the ganglion cells of the **profundus nerve** [Fig. 9-8(A)]; the possibility exists that the profundus ganglion

also contains some cells derived from neural crest. The profundus is a sensory nerve, supplying a surface area on the snout of fishes. In the coelacanth *Latimeria*, the profundus nerve additionally supplies the mucosa of a series of rostral tubes that contain separately innervated electroreceptors. The profundus nerve has no motor component, as does the more caudal trigeminal nerve, but it can be considered to be the dorsal nerve of the first head segment. In mammals, in which the profundus nerve is called the **ophthalmic branch of the trigeminal nerve**, the ganglia of the profundus and trigeminal nerves merge. No ventrolateral nerve derived from an epibranchial placode is present in the first head segment. Dorsolateral nerves will be discussed in conjunction with the third head segment.

The Second Head Segment

Somitomeres 3 and 4 are the paraxial mesoderm of the second model head segment. Somitomere 3 gives rise to the dorsal oblique muscle of the eye. The dorsal oblique is innervated by cranial nerve IV, the **trochlear nerve**, which is the ventral nerve of the second (mandibular) model head segment [Fig. 9-8(A)]. Somitomere 4 gives rise to the muscles of the jaw. The dorsal nerve of this segment is the **trigeminal nerve**, cranial nerve V, which has a branchiomic somatic motor component innervating the muscles of the jaw and a somatic sensory component. The ganglion cells of the sensory component of this dorsal nerve lie in the proximal part of the trigeminal ganglion and arise from both neural crest and the trigeminal placode [Fig. 9-8(A)]. The second head segment, like the first, lacks ventrolateral nerves derived from placodes. Dorsolateral nerves will be discussed in conjunction with the third head segment.

The Third Head Segment

The paraxial mesoderm of the third (hyoid) model head segment is derived from somitomeres 5 and 6. Somitomere 5 gives rise to the lateral rectus muscle of the eye. The lateral rectus is innervated by the ventral, somatic motor nerve of the third head segment, cranial nerve VI, the **abducens nerve** [Fig. 9-8(A)], which courses rostrally to reach the muscle. Somitomere 6 gives rise to the branchiomic muscles of the face. These muscles are innervated by the motor fibers in the dorsal nerve of the third head segment, the **dorsal facial nerve**, cranial nerve VII_D. Like the trigeminal nerve of the second head segment, the dorsal facial nerve also has a somatic sensory component. The ganglion cells for this sensory component are presumably derived from neural crest and lie in the proximal part of the ganglion of the nerve.

The third head segment is the central-most segment for nerves derived from dorsolateral placodes [Fig. 9-8(B)]. The dorsolateral series of placodes gives rise to the receptors and ganglion cells of a multiple set of nerves. Three **preotic placodes** (Table 9-3) give rise to the ganglion cells and receptors of three **lateral line nerves**—**anteroventral** (LL_{AV}), **anterodorsal** (LL_{AD}), and **otic** (O)—for electroreception and/or mechanoreception. An **octaval placode** gives rise to the receptors within the membranous labyrinth of the inner ear and to the ganglion cells of the vestibular and cochlear rami

TABLE 9-3. Lateral Line and Octaval Placodes and Nerves

Placodes	Nerves
Preotic	Anteroventral lateral line Anterodorsal lateral line Otic lateral line
Octaval	Cochlear ramus of eighth Vestibular ramus of eighth
Postotic	Middle lateral line Supratemporal lateral line Posterior lateral line

of the **octaval** (VIII) **nerve**. The **vestibular ramus** carries balance and position senses, and the **cochlear ramus** carries hearing. Three **postotic placodes** give rise to the ganglion cells and receptors of three additional lateral line nerves—**middle** (LL_M), **supratemporal** (LL_{ST}), and **posterior** (LL_P). We have illustrated the six lateral line placodes and the octaval (vestibulocochlear) placode as primarily associated with the third segment. Alternatively, as shown in Table 9-2, these dorsolateral placodes may be serially related to a number of head segments, such that the anterodorsal placode is the dorsolateral placode of the first head segment, the anteroventral placode is of the second, the otic and octaval placodes are of the third, the middle is of the fourth, and the supratemporal and posterior are of the fifth and more caudal segments. Further research is needed to clarify whether such registry of dorsolateral placodes and rhombomeres exists.

The third head segment also has a ventrolateral nerve, derived from a ventrolateral, epibranchial placode, which innervates the set of taste buds that are derived from ectoderm (on the anterior two-thirds of the tongue and, in some fishes, on the outer surface of the body). This nerve is the **ventrolateral facial nerve** [VII_{VL}, in Fig. 9-8(B)]. The neuron cell bodies of the axons of this nerve lie in the distal part of the ganglion of the facial nerve and are derived from placode.

The Fourth Head Segment

There is only one somitomere associated with the fourth model head segment. Within this segment, somitomere 7 gives rise to muscle associated with the first branchial arch (third visceral arch). These muscles are innervated by branchiomic somatic motor fibers in the **dorsal glossopharyngeal nerve**, cranial nerve IX_D. The dorsal glossopharyngeal nerve also has a somatic sensory component, and neural crest cells give rise to the ganglion cells of these sensory fibers in the proximal ganglion of the nerve. The dorsal glossopharyngeal nerve is thus the dorsal nerve of the fourth head segment [Fig. 9-8(A)], and somitomere 7 resembles the more caudal of the two somitomeres present in the more rostral head segments. A more rostral somitomere apparently does not develop in the fourth head segment, and, correspondingly, no ventral, purely somatic motor nerve is present.

The dorsolateral nerve of the fourth head segment may be the middle lateral line nerve, as discussed above. The ventro-

lateral nerve of this segment, derived from an epibranchial placode, is the **ventrolateral glossopharyngeal nerve** (IX_{VL}). The ganglion cells for the sensory fibers are derived from placode and lie in the distal ganglion of the nerve [Fig. 9-8(B)]; they innervate taste buds derived from endoderm on the caudal one third of the tongue.

The Fifth Head Segment

A series of somites are present caudal to somitomere 7, which gives rise to muscles of the larynx and tongue, as well as to hypobranchial muscles (those below the gill arches in the neck), in the fifth model head segment. The ventral, somatic motor nerve is derived from the neural tube of this segment and is cranial nerve XII, the **hypoglossal nerve** [Fig. 9-8(A)]. The hypoglossal nerve innervates the muscles of the tongue in tetrapods. The **dorsal vagus nerve**, cranial nerve X_D, is the dorsal nerve of the fifth head segment. The external, branchiomeric muscles of this head segment are innervated by its branchiomeric somatic motor component. The ganglion cells of the sensory component of the dorsal vagus nerve are derived from neural crest and lie in the proximal ganglion of the nerve. The **accessory nerve**, cranial nerve XI (not included in Table 9-2), is also associated with the fifth head segment but is not as clearly understood. It is present in a wide range of vertebrates rather than being present only in amniotes as previously believed. In birds and mammals, the accessory nerve is a composite nerve, with a spinal motor nucleus that is plesiomorphic for at least jawed vertebrates and a bulbar portion of the nucleus derived from the vagus. The latter contributes to the innervation of the larynx.

The supratemporal and posterior lateral line placodes may supply the dorsolateral nerve component for the fifth (and more caudal) head segment, as discussed above. The ventrolateral, epibranchial series of placodes gives rise to a ventrolateral nerve of the fifth head segment, the **ventrolateral vagus nerve** (X_{VL}). The ganglion cells of this nerve innervate taste buds for this head segment, which, like those innervated by IX_{VL}, are derived from endoderm. They are derived from placode and lie in the distal ganglion of the nerve [Fig. 9-8(B)].

We have not included some cranial nerve components in this analysis for the sake of the clarity of the overall pattern. As in the spinal cord segmental nerves, there are also autonomic and visceral sensory components of cranial nerves. In addition, there are efferent components in a number of the sensory cranial nerves that terminate on the sensory receptor cells. These additional components, however, do not negate the overall scheme presented above.

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10

Functional Organization of the Cranial Nerves

INTRODUCTION

The segmental organization of the cranial nerves, as discussed in Chapter 9, forms the basis for the classification and organization of the cranial nerves presented in this chapter. Table 10-1 is a list of all the cranial nerves in vertebrates. The reader should note that not all animals possess all of these nerves; many nerves and/or individual components of nerves are absent in various species depending on how they have become adapted to their particular environments. A classification of the sensory (afferent) and motor (efferent) cranial nerves according to embryological origin and nerve type is presented in Tables 10-2 and 10-3, respectively. This new classification is tentative, since, as discussed in Chapter 9, the embryological origin of all the neurons in the various cranial nerve ganglia has yet to be confirmed experimentally. It represents, however, a radical departure from the traditional classification of cranial nerves as might be found in a medical school textbook of human neuroanatomy. This new approach to classification is necessary for a comparative and evolutionary approach to the cranial nerves because many nerves and/or their components are not found in humans. Moreover, this new classification is consistent with the recent findings about the embryological origins of these nerves.

An inspection of Tables 10-2 and 10-3 reveals that a number of the nerves appear in more than one cell. The reason is that some cranial nerves, such as the trigeminal (V) and the dorsal vagus (X_D), which belong to the dorsal group of cranial nerves (see Chapter 9), contain both afferent and efferent fibers. Others, such as the oculomotor (III) and abducens (VI) nerves, which belong to the ventral group of cranial nerves,

have only efferent fibers. Until fairly recently, anatomists believed that sensory nerves, such as the optic (II) and the octaval (VIII), contained only sensory afferent fibers. We now know that a number (and possibly all) of the sensory cranial nerves also contain some efferent fibers, which produce changes in the sensitivity of sensory receptors. These efferent fibers have not been included in Table 10-2, however, as they do not affect the classification scheme and are not currently treated as separate components.

Table 10-4 lists all of the individual components of all the cranial nerves. This table includes information presented in the two preceding tables on the modality or innervation pattern of each component, the new classification of each component based on its embryological derivation, and, in cases of the motor nerves, the embryological origin of the muscles that are innervated. This table also includes the traditional classification given for each component. As discussed in Chapter 9, the special categories included here have been invalidated by recent findings. Nonetheless, they are shown here for reference and for comparison with other texts that still employ them.

THE CRANIAL NERVES AND THE SPINAL CORD

Some of the cranial nerves share a number of characteristics of the spinal nerves. The dorsal cranial nerves have sensory components with ganglia, similar to the dorsal roots of the spinal cord. The ventral cranial nerves have motor roots that arise from large, motor neuron cell bodies similar to the ventral

TABLE 10-1. The Cranial Nerves of Vertebrates

Symbol	Name	Innervation
T	Terminalis	Nasal septum
I	Olfactory	Olfactory epithelium
VN	Vomeronasal	Vomeronasal organ
II	Optic	Retina
E	Epiphyseal	Pineal; parietal eye
III	Oculomotor	Internal and external eye muscles
P	Profundus	Skin of the snout
IV	Trochlear	External eye muscle
V	Trigeminal	Jaw muscles; touch to face, snout and oral cavity
VI	Abducens	External eye muscle
VII _D	Dorsal facial	Facial muscles; salivary and tear glands
VII _{VL}	Ventrolateral facial	Taste buds
VIII	Octaval or vestibulocochlear	Vestibular organs; cochlea; lagena
LL	Lateral line (6 nerves)	Lateral line organs
IX _D	Dorsal glossopharyngeal	Pharynx; salivary glands
IX _{VL}	Ventrolateral glossopharyngeal	Taste buds
X _D	Dorsal vagus	Viscera of thorax and abdomen; larynx; pharynx
X _{VL}	Ventrolateral vagus	Taste buds
XI	Spinal accessory	Neck and shoulder muscles; larynx
XII	Hypoglossal	Tongue; syrinx

TABLE 10-2. A Classification of the Sensory (Afferent) Cranial Nerve Components of Vertebrates Based on Embryological Origins

Predominant Embryological Origin	Nerve Type	Nerve(s) or Nerve Component(s)	Modality and/or Innervation
Neural crest	Visceral	T, IX _D , X _D	? and Visceral surfaces of head and body
	Somatic	VII _D , IX _D , X _D	Skin in and near ear
Neural crest and placodes	Somatic	V, P	Somatic muscles and much of the skin surface of head
Placodes	Forebrain placodal	I, VN	Olfactory
	Dorsolateral placodal	VIII, LL	Hair cells and electroreceptors
	Somatic and Visceral: Ventrolateral placodal	VII _{VL} , IX _{VL} , X _{VL}	Taste
Neural tube	Part of central nervous system	II	Light detection from retina
		E	Light detection from epiphyseal structure(s)

TABLE 10-3. A Classification of the Motor (Efferent) Cranial Nerve Components of Vertebrates Based on Embryological Origins

Predominant Embryological Origin	Nerve Type	Nerve or Nerve Component	Innervated Target
Neural tube	Visceral (Parasympathetic)	III, VII _D , IX _D , X _D	Glands, intraocular muscles, smooth muscles of body viscera, and cardiac muscles
		III, IV, VI	Extraocular muscles and eyelid
	Somatic	V, VII _D , IX _D , X _D , XI	Branchiomeric muscles
		XII	Muscles of the tongue

TABLE 10-4. Comparison of Classification Based on Embryological Origin and Traditionally Used Classification

Nerve(s) or Nerve Component (s)	Modality and/or Innervation	Embryologically Based Classification	Traditional Classification ^a
T	?	Forebrain Neural Crest-derived	—
I, VN	Olfactory	Forebrain placodal	—
II, E	Light detection	Central Nervous System	—
III	Extraocular muscles and eyelid	Somatic Efferent	GSE
	Parasympathetic	Visceral Efferent	GVE
IV	Extraocular muscle	Somatic Efferent	GSE
V, P	Sensory to skin and muscles	Somatic Afferent	GSA
V	Muscles of jaw	Somatic Efferent—Branchiomeric	SVE
VI	Extraocular muscle	Somatic Efferent	GSE
VII _D ^b	Sensory to skin	Somatic Afferent	GSA
	Motor to hyoid arch muscles	Somatic Efferent—Branchiomeric	SVE
	Parasympathetic	Visceral Efferent	GVE
VII _{VL}	Taste	Somatic Afferent	SVA
VIII, LL	Hair cells and electroreceptors	Somatic Afferent	SSA
IX _D	Sensory to skin	Somatic Afferent	GSA
	Sensory to throat	Visceral Afferent	GVA
	Motor to pharynx muscle	Somatic Efferent—Branchiomeric	SVE
	Parasympathetic	Visceral Efferent	GVE
IX _{VL}	Taste	Visceral Afferent	SVA
X _D	Sensory to skin	Somatic Afferent	GSA
	Sensory to viscera	Visceral Afferent	GVA
	Motor to pharynx and larynx muscles	Somatic Efferent—Branchiomeric	SVE
	Parasympathetic	Visceral Efferent	GVE
X _{VL}	Taste	Visceral Afferent	SVA
XI	Muscles of neck and shoulder; larynx	Somatic Efferent—Branchiomeric	SVE
XII	Muscles of tongue	Somatic Efferent	GSE

^a GSA, General Somatic Afferent; GVA, General Visceral Afferent; GVE, General Visceral Efferent; GSE, General Somatic Efferent; SSA, Special Somatic Afferent; SVA, Special Visceral Afferent; SVE, Special Visceral Efferent.

^b Some sources on human neuroanatomy list a GVA component for VII_D while others do not. In this book, we have elected to treat VII_D as having only four components rather than five.

roots of the cord. Like the spinal nerves, segmental organization of the cranial nerves exists in the pattern of innervation of peripheral structures. The notion that the lower brainstem is a continuation of the spinal cord with the same general organization is strengthened by the continuity of most of the sensory cell columns of the dorsal horn of the cord with sensory cell columns of the lower brainstem and by the continuity of the motor cell columns of the ventral horn of the cord with motor cell columns of the lower brain stem (Fig. 10-1).

THE ORGANIZATION OF SENSORY AND MOTOR COLUMNS OF THE CAUDAL BRAINSTEM

Sensory and motor components of cranial nerves are segmentally organized, and the points at which they enter or leave the brain reflect their developmental history. Separate motor nuclei are present for most of the various motor cranial nerves. In contrast, a large number of nerves exist by which sensory

axons can enter the brain, but a unique, separate nucleus is not always present in the brain for every sensory component of each nerve. The zones of termination are in fact relatively few and are related to the particular system rather than to the individual components of individual nerves. For example, all somatic afferent neurons traditionally classified as general (i.e., those carrying information about pain, temperature, touch, pressure, muscle stretch, and the position of joints) entering the brainstem, no matter by which nerve they enter—trigeminal (V), dorsal facial (VII_D), dorsal glossopharyngeal (IX_D), or dorsal vagus (X_D)—terminate in a sensory cell column known as the general somatic afferent column, which is continuous with the dorsal horn of the spinal cord (Figs. 10-1 and 10-2). In a similar manner, the visceral afferent neurons (i.e., those carrying information about pain, temperature, pressure, and muscle stretch from the viscera in the body) that enter the brainstem, whether they enter through IX_D or X_D, terminate in the general visceral afferent column, which is likewise continuous with the dorsal horn (Figs. 10-1 and 10-2). All of the ventrolateral (epibranchial) placodal afferent neurons carrying taste information, whether they enter through VII_{VL}, IX_{VL}, or

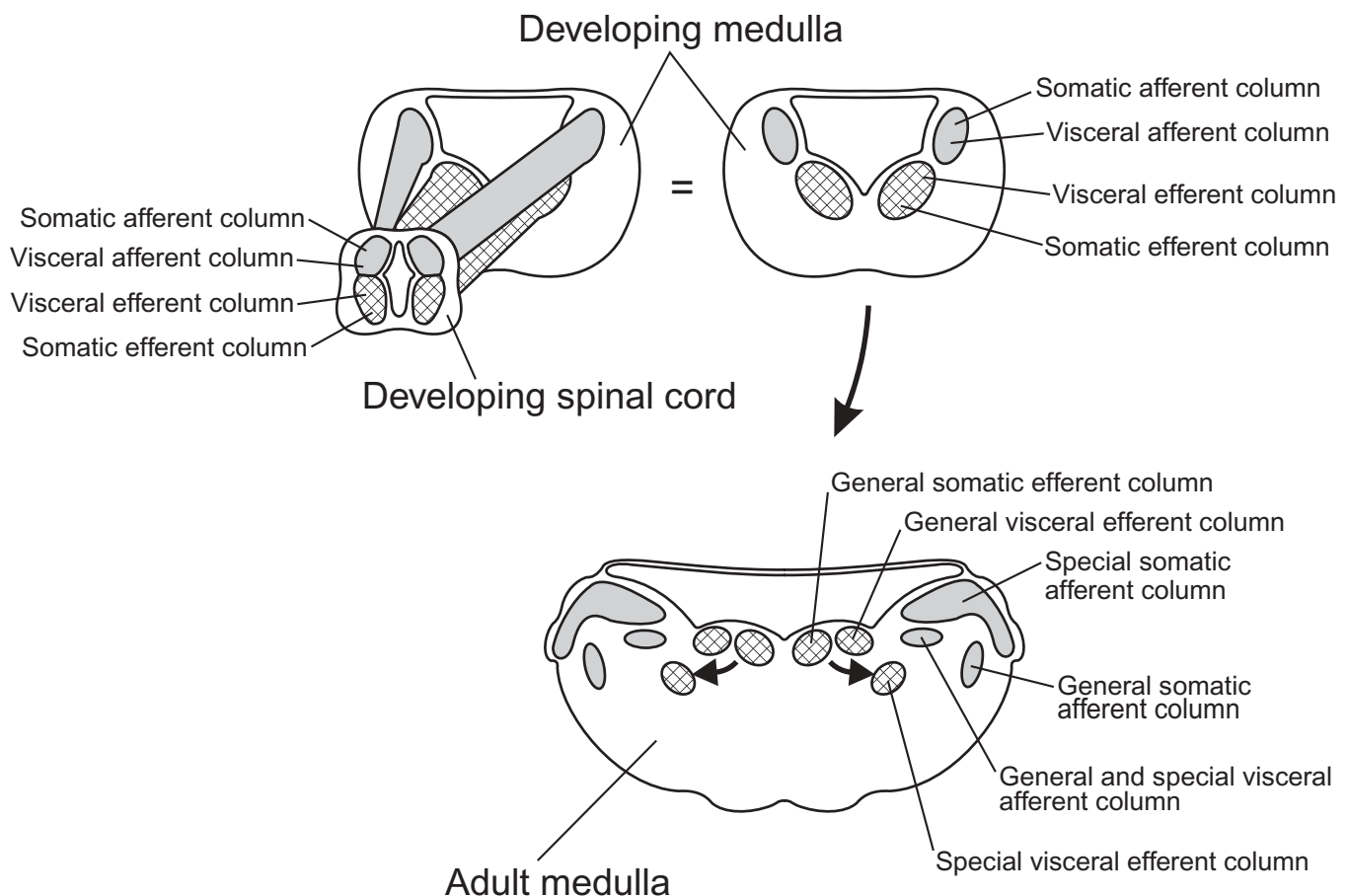


FIGURE 10-1. Schematic drawings to show the continuity of cell columns in the spinal cord with those in the medulla. Top left: developing brainstem and spinal cord are shown with the rostrocaudal continuity of the alar plate cell columns (in gray) and the basal plate cell columns (cross-hatched). Top right: A transverse section through just the developing medulla. Bottom: adult configuration of the medulla, with the alar and basal plates each comprising several columns.

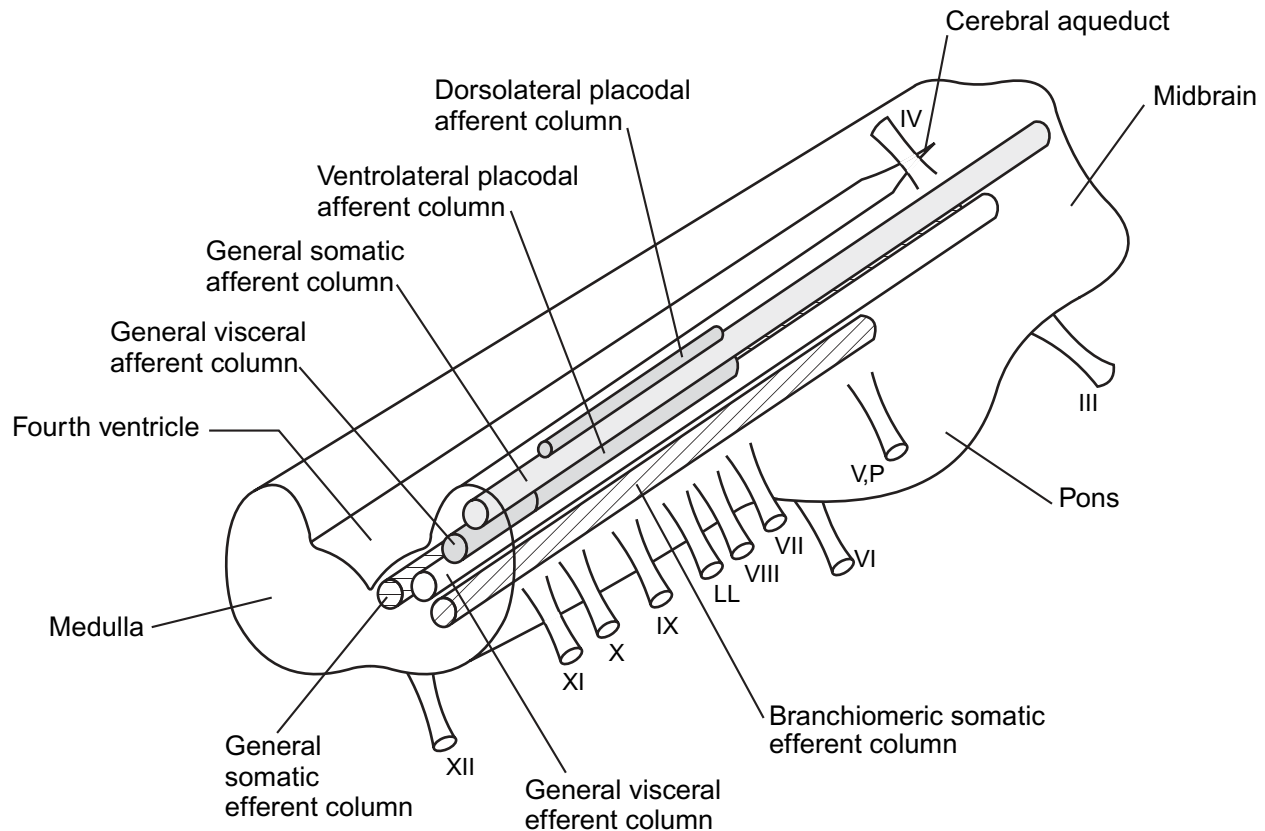


FIGURE 10-2. Schematic drawing of a dorsolateral perspective on a generalized brainstem. All of the sensory and motor cell columns are shown for orientation. Rostral is toward the upper right. It is important to realize that the individual nuclei that constitute these columns are not all in continuity rostrocaudally but rather lie separately along the line of the column. This generalized drawing is a composite of different vertebrate groups. It includes the bulge of the pons (under cranial nerve V,P) and cranial nerves XI and XII, as in amniotes, as well as a single lateral line nerve to represent the six lateral line nerves present in most anamniotic aquatic vertebrates.

X_{VL} , terminate in the rostral extension of this same visceral sensory column. As we will again note below, however, the “visceral” designation is not apt for VII_{VL} since the taste buds that it innervates are derived from ectoderm. Columnar continuity between the spinal cord and the brainstem does not occur for all cranial nerve systems; all of the dorsolateral placodal afferent neurons terminate within their column (Fig. 10-2), which is unique to the head.

Figure 10-2 also shows the various cell columns for the motor components of cranial nerves. These columns can be distinguished according to the pattern of innervation. The cranial nerve motor components traditionally classified as general lie close to the midline and in the dorsal part of the tegmentum or medulla in the general somatic efferent column, and their axons exit the brain on its ventral surface via the ventral series of nerves. The motor components that innervate the branchiomeric muscles of the visceral arches tend to lie in a more ventrolaterally migrated position in the traditionally called “special” “visceral” efferent column, which is actually the branchiomeric somatic efferent column. Their axons exit the brain via the trigeminal nerve and the more caudally lying series of dorsal nerves. Parasympathetic components exit the brain from

the general visceral efferent column either through ventral or dorsal nerves.

Afferent Columns of the Brainstem

General Somatic Afferents. In Figure 10-3(A), somatic afferent fibers from the face and head that enter the brainstem through the trigeminal (V), profundus (P), dorsal facial (VII_D), dorsal glossopharyngeal (IX_D), and dorsal vagus (X_D) nerves all are shown terminating among the cells of the general somatic afferent column. This column includes the **principal** and the **descending** (or **spinal**) **nuclei of the trigeminal nerve** (V). The latter nucleus is so named since, from its rostral-most level, it extends (or “descends”) caudally to upper spinal cord levels.

The profundus nerve is a distinct nerve only in fishes. It innervates the skin on the dorsal, rostral part of the head and on the snout. In mammals, the profundus nerve is the same as the most rostral (ophthalmic) branch of the trigeminal nerve. Further research is needed to fully clarify the trigeminoprofundal relationship; some research indicates that the trigeminal ganglion arises from neural crest, whereas the profundus gan-

glion cells are of placodal origin. Additional studies on a variety of vertebrate species are needed to answer this question. The central connections of the profundus nerve, particularly in nonmammalian vertebrates, are not well worked out; a comparative study of them would add to our understanding of the development of the head and the organization of the trigeminal sensory system as well.

General Visceral Afferents. Figure 10-3(A) also shows visceral afferent fibers from the viscera of the thorax, abdomen,

and throat region entering the brainstem via cranial nerves IX_D and X_D. The part of the visceral afferent column in the caudal-most part of the brainstem where these fibers terminate is called **nucleus solitarius**.

Ventrolateral Placodal Afferents. Ventrolateral, epibranchial placodal afferent fibers carrying taste information [Fig. 10-3(B)] terminate in a cell column that lies rostral to the general visceral afferent column. Because taste was previously regarded as a special sense, this part of the visceral afferent column has

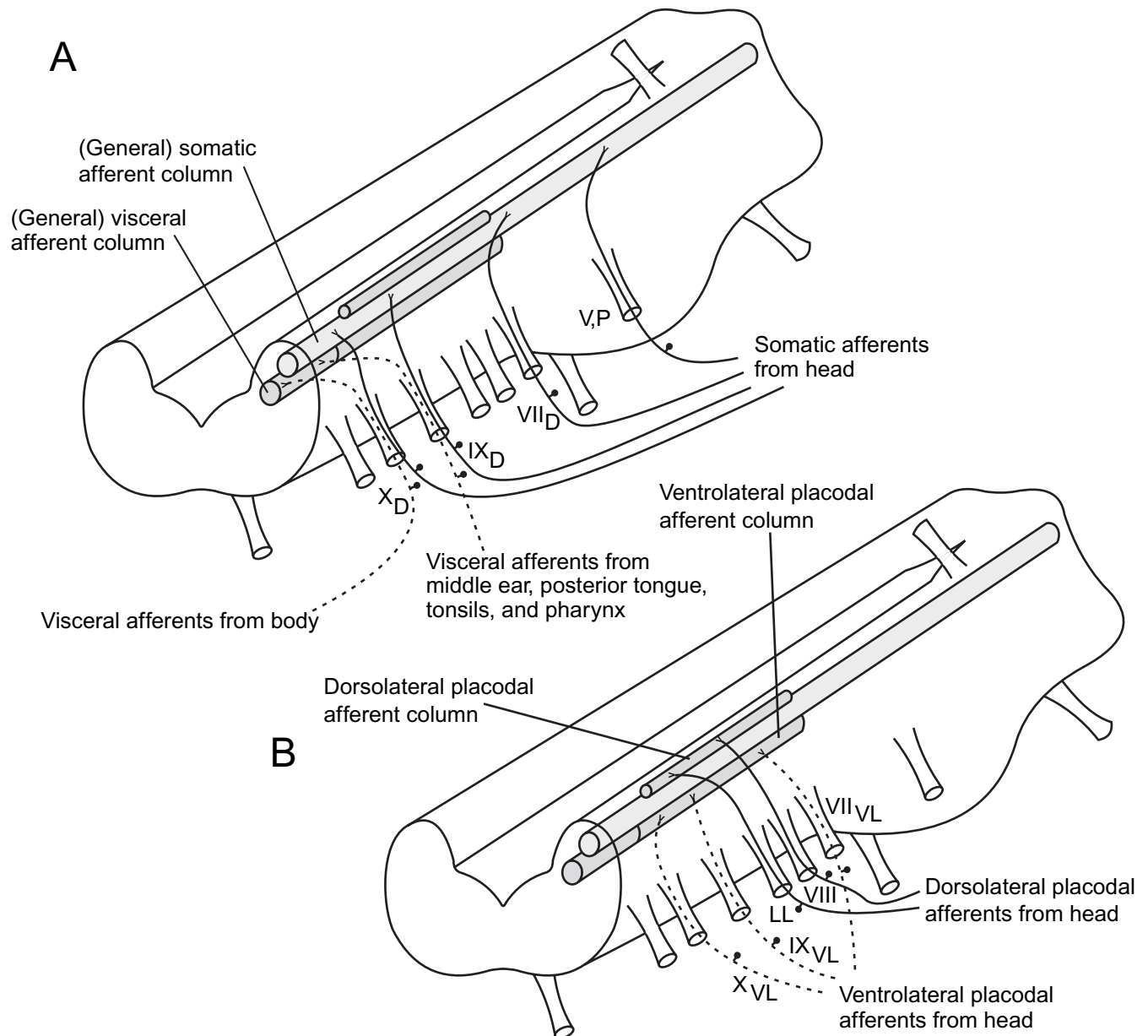


FIGURE 10-3. Schematic drawings of the caudal brainstem, extracted from the generalized template shown in Fig. 10-2, to show the major afferent cell columns in relation to the cranial nerves. Rostral is toward the upper right. A: general visceral and general somatic afferent cell columns. B: dorsolateral and ventrolateral (epibranchial) placodal afferent cell columns. The latter cranial nerves were previously classified as special somatic afferent and special visceral afferent, respectively.

traditionally been designated as the special visceral sensory column. It is in fact a rostral continuation of the general visceral afferent column. Taste buds are derived from different embryological sources: those innervated by VII_{VL} are derived from ectoderm and lie on the anterior two-thirds of the tongue. Thus, the appropriate designation for VII_{VL} is somatic afferent. More caudally lying taste buds on the caudal one-third of the tongue and the surrounding throat region are derived from endoderm, so the designation of visceral is appropriate for their innervation by IX_{VL} and X_{VL}. The entire column has previously been referred to as nucleus solitarius, but the zone of termination of the taste afferents is now recognized as a separate nucleus called the **gustatory nucleus**. It receives the ventrolateral placodal afferents from the ventrolateral facial (VII_{VL}), ventrolateral glossopharyngeal (IX_{VL}), and ventrolateral vagus (X_{VL}) nerves.

Dorsolateral Placodal Afferents. These afferent cranial nerves comprise the octaval and lateral line nerves. They were previously classified as special somatic afferent.

The octaval nerve has vestibular and cochlear divisions that are both derived from the dorsolateral octaval placode, as is the otic capsule. Octaval nerve fibers terminate within a **dorsolateral octaval column** that lies near the somatic afferent column [Fig. 10-3(B)]. The dorsolateral octaval column contains a number of individual nuclei. Vestibular receptors are located in parts of the inner ear called the utricle, saccule, and semicircular canals. They detect acceleration and position relative to gravity in order to maintain equilibrium and orientation in space. The vestibular nerve projects to nuclei within the dorsolateral placodal column called the **vestibular nuclei**. These nuclei lie within the pons. The cochlear ramus of the eighth cranial nerve carries auditory information from the cochlea in the inner ear. The auditory fibers terminate in nuclei in the dorsolateral placodal column of the pons that generally are called the **cochlear nuclei**. The fibers terminate in the nuclei in an ordered manner so that there are maps of lower to higher tones within the nuclei. This tonotopic organization is maintained in projections to auditory areas in the more rostral parts of the brain.

Most nonamniote aquatic vertebrates have six lateral line nerves, including lampreys, some cartilaginous and ray-finned fishes, and some amphibians. The six lateral line nerves, which innervate electrosensory and/or mechanosensory receptors, are the anterodorsal, anteroventral, otic, middle, supratemporal, and posterior, although not all six are present in all species that have a lateral line system. These nerves are derived from the dorsolateral series of placodes, as is the octaval nerve, and they terminate in nuclei of the dorsolateral placodal column [Fig. 10-2(B)]. Electroreception and a lateral line-type of mechanoreception have recently been found to be present in monotremes and may be present in one or more placental mammals as well, but these senses in mammals evolved independently and are innervated by the trigeminal nerve.

The lateral line nerves in aquatic anamniotes serve a series of organs known as the lateral line organs, which are arrayed in lines that generally lie in shallow grooves, or canals, several of which are on the surface of the head and one of which runs the length of the body. The lateral line canals contain receptors

(see Chapter 2) that detect the displacement of water across the animal's head and body, as would be caused by another animal swimming nearby. These receptors are called **neuromasts** and are characterized by a hair-cell epithelium that is surrounded by nonneural support cells and mantle cells. They are said to be mechanoreceptive.

A second class of receptors, which are present in some species, are electroreceptive. These receptors are of two similar types, known as **ampullary organs** and **tubercular organs** (see Chapter 2). They are both formed by a receptor epithelium at the base of a small, encapsulated pouch that is connected to the surface of the epidermis by a small canal or pore. The electroreceptive, lateral line system is used to detect the weak electrical fields that are generated around living organisms. In those cartilaginous fishes, such as the torpedo, and in those ray-finned fishes, such as the electric eel, that generate more substantial electric fields around themselves, these organs serve to detect these fields. Many species of cartilaginous and ray-finned fishes that do not generate the stronger electric fields are, nevertheless, capable of detecting such fields. This electroreceptive sense is useful in the detection of prey in murky waters or just beneath the surface of sand or mud at the bottom of the water.

Efferent Columns of the Brainstem

General Visceral Efferents. The **visceral efferent column** is a continuation of the visceral efferent column of the spinal cord (Fig. 10-1), which in tetrapods is called the **intermediolateral cell column**. This column of cells from spinal cord to caudal brainstem comprises the **autonomic nervous system**. The cranial nerve components (together with those of the sacral spinal cord) constitute the **parasympathetic division**, and those of the thoracic and lumbar levels of the spinal cord constitute the **sympathetic division**. The cranial nerve components of the autonomic nervous system in the head exit the brain via cranial nerves III, VII_D, IX_D, and X_D (Fig. 10-4). They innervate the internal eye muscle that contracts the pupil of the eye and the muscle that controls accommodation (the focusing of the eye on close objects), and they innervate the salivary glands and tear glands in tetrapods, as well as the internal organs of the thorax, abdomen, and pelvis. These parasympathetic components are traditionally classified as general visceral efferent.

Somatic Efferents. The **general somatic efferent column** (Fig. 10-4) is a continuation of the motor neuron column of the ventral horn of the spinal cord. Just as the motor neurons of the spinal cord control skeletal muscles of the body, so do their brainstem counterparts control the skeletal muscles of the head. The oculomotor (III), trochlear (IV), and abducens (VI) nerves together control the external eye muscles, which move the eye in its socket. The oculomotor nerve also contributes to the innervation of the eyelid. In tetrapods, the hypoglossal nerve (XII) controls the muscles of the tongue. These four ventral nerves are traditionally grouped as general somatic efferents. The **branchiomeric somatic efferent column** (Fig. 10-4) also may be regarded as a continuation of the ventral horn of the spinal cord. The motor neurons of this column that exit via the trigeminal (V) nerve control the

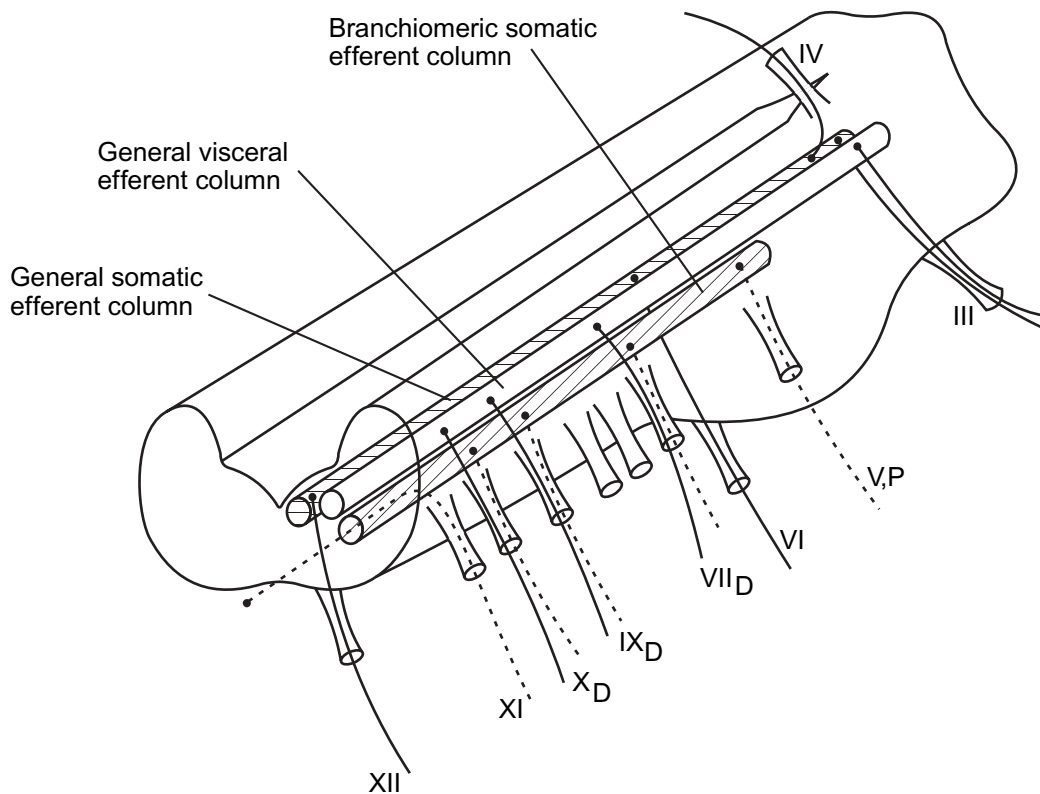


FIGURE 10-4. Schematic drawing, extracted from the generalized template shown in Fig. 10-2, illustrating the motor columns of the caudal brainstem. Rostral is toward the upper right.

muscles of the jaws, and the motor neurons of the dorsal facial (VII_D) nerve control the muscles of the face, such as lips, eyelids, cheeks, and nostrils, in those animals that have such structures and are capable of moving them. The motor neurons of the dorsal glossopharyngeal (IX_D), dorsal vagus (X_D), and accessory (XI) nerves control the muscles of the throat and neck. These five nerves that innervate the branchiomeric muscles have traditionally been classified as originating in the special visceral efferent column. As discussed in Chapter 9, they are, however, neither special nor visceral, since the branchiomeric muscles have the same embryological derivation as do the extraocular and tongue muscles and are likewise under voluntary control and of a histological structure that is consistent with their somatic nature.

FIVE CRANIAL NERVES ROSTRAL TO THE BRAINSTEM

Five nerves remain to be discussed in this introduction to the cranial nerves: the optic nerve (II), the epiphyseal nerve (E), and three more rostral nerves—the olfactory nerve (I), vomeronasal nerve (VN), and terminal nerve (TN). All five of these nerves are in the forebrain. These nerves are exceptions to the general rules of cranial nerve termination in that their sites of termination are not at all related to the sensory columns of the brainstem.

Because the retina of the eye and the sensory receptors in the epiphysis are actually outgrowths of the brain, the optic nerve (II) and the epiphyseal nerve (E), which carry information from the receptors to the brain, are true pathways of the central nervous system rather than peripheral nerves, as are the cranial nerves of the caudal brainstem. The retina of the eye contains a number of receptors and neuron types arranged in a complex organization similar to that found in the central nervous system, so that a considerable amount of processing of the visual input goes on in the retina before the optic nerve conducts it to the brain. The optic nerve (II) terminates in a number of nuclei located in the **thalamus** and **hypothalamus**, which lie in the diencephalon, and in the **optic tectum**, which lies in the roof of the midbrain. The epiphyseal nerve comprises either one or two divisions in most vertebrate groups: one from the pineal part of the epiphysis and, sometimes, one from the more rostral part of the epiphysis (see Chapter 21). The one or two divisions of the epiphyseal nerve terminate in the **epithalamus**, which is the most dorsal part of the diencephalon.

The axons of the olfactory nerve (I) are, in some cases, among the shortest of the cranial nerve axons. The olfactory receptors are located in the mucous membranes that lie deep within the nose. The axons of the olfactory nerves travel through small openings in the roof of the nasal passage to the **olfactory bulb**, or **main olfactory bulb**, which lies just above. The main olfactory bulb is an extension of the cerebral hemisphere, which is located close to the olfactory receptors.

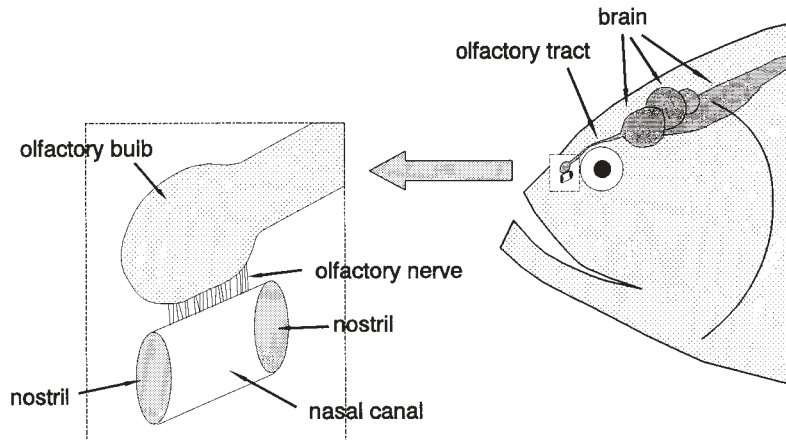


FIGURE 10-5. Schematic drawing of the olfactory afferent system in the head of a fish (right), with the area of the olfactory nerve and bulb enlarged (left).

It is connected to the main body of the cerebral hemisphere by a band of axons called the **olfactory tract** (Fig. 10-5). The length of the tract depends on the length of the animal's snout. In animals with a long snout, that is, those in which the nostrils are located relatively far rostral to the eyes, such as alligators, many hoofed mammals, and many fishes, the olfactory tract can be quite long. In short-snouted animals, such as many primates, the tract is rather short. In many birds, in which the nostrils are quite close to the eyes, the tract *per se* does not exist, and the main olfactory bulb is connected directly to the cerebral hemisphere. The olfactory nerve is derived from the rostrally lying olfactory placode, as is the vomeronasal nerve.

The vomeronasal nerve (VN) is functionally similar to the olfactory nerve. It arises from a sensory area inside the nose called the **organ of Jacobson** and projects to a structure that lies next to the main olfactory bulb called the **accessory olfactory bulb**. The vomeronasal system is best developed in squamate reptiles.

Like the receptors for taste, the olfactory and vomeronasal receptors are sensitive to chemical substances present in the environment. In air-breathing animals, the chemicals to which the olfactory receptors are sensitive are volatile and disperse through the air, whereas the gustatory (taste) receptors are sensitive to chemicals that are water soluble. However, in aquatic animals, chemicals that are olfactory stimuli must also be water soluble.

The final cranial nerve on our list is the terminal nerve (TN). This nerve is present in most or all jawed vertebrates and is embryologically derived from cranial neural crest tissue. The terminal nerve was long thought to be absent in birds, but recent evidence suggests that it is present in this group as well as in other vertebrate groups. In aquatic animals, the terminal nerve dendrites are known to innervate the nasal septum, but the central connections of the terminal nerve are quite different from those of the olfactory and vomeronasal nerves. A unique characteristic of the terminal nerve is that many of its fibers contain a hormone called **luteinizing-hormone releasing hormone (LHRH)**, also known as **gonadotrophin-releasing hormone (GnRH)**. This hormone is also present in some of the cells in the hypothalamus that project to the pitu-

itary. This hormone causes the anterior pituitary to secrete luteinizing hormone, which controls the secretion of sex hormones from the testes and ovaries. A most peculiar property of the GnRH-positive terminal nerve fibers in fishes is that some of them turn from the terminal nerve into the optic nerve and terminate in the retina. The functional role of this olfactoretinal pathway in reproductive or other behaviors has not yet been elucidated.

GENERAL CONSIDERATIONS

A feature of all of the cranial nerves, one that is shared with structures in the central nervous system, is the relationship between the size and development of the nerve and the extent to which it is used. In animals with a well-developed olfactory sense, such as sharks and some mammals, the olfactory bulb is enormous in comparison to those animals with a more modest sense of smell. Similarly, animals with a prominent snout that is used for exploration of the environment with the sense of touch have very large sensory branches of their trigeminal nerves, as do animals in which the trigeminal nerve is specialized for other sensory uses, such as electroreception, mechanoreception, and infrared detection (see Chapter 11). Those animals with powerful jaws have large motor branches of their trigeminal nerves. Ray-finned fishes have an excellent gustatory system, but in certain species, especially goldfishes and catfishes, the gustatory system reaches an extraordinarily high degree of development. These fishes have many thousands of taste buds, not only in the mouth but on the head and all over the body as well. The gustatory nerves (VII_{VL}, IX_{VL}, and X_{VL}) are extremely large, and the central structures and cell groups that are associated with these nerves rival those of the visual system in size and complexity of organization. In subsequent chapters, we will discuss each of the cranial nerves in greater detail and will point out how the structure and organization of these nerves and the cell populations that they interact with are intimately related to how animals survive in their environments.

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Sensory Cranial Nerves of the Brainstem

INTRODUCTION

Animals detect and respond to the physical properties of their internal and external environments by means of their sensory systems. The particular sensory systems that any given species possesses are a reflection of its unique adaptation to its particular environment. Sensory systems may be classified into three broad categories: chemical senses, which comprise taste, smell, and general chemical sensitivity; mechanical senses, such as hearing and touch; and electromagnetic senses, such as vision, electroreception, and infrared detection. In addition to detecting the external environment, animals possess a number of interoceptors. Chemical interoceptors include those for blood chemistry, such as for monitoring glucose, oxygen, pH, various salts, and other blood constituents. The reader is referred to Table 2-3, which lists the three major categories of stimuli and the location of their receptors in the body. The reader should be aware that this is not an exhaustive list, and further subdivisions of various categories can be made.

The sensory cranial nerves of the brainstem fall into three distinct categories: the dorsal cranial nerve sensory components of the trigeminal nerve that carry somatosensory sensation for the head, the ventrolateral placodal nerves that carry taste, and the dorsolateral placodal nerves that carry the lateral line and octaval senses. As discussed in Chapter 9, each of these three categories represents a developmentally distinct component of the neuromeric segments. The sensory cranial nerves of the forebrain are discussed in later chapters. For reference, Table 11-1 shows the traditional and new classifications, the location of the bipolar sensory neurons, the location of the first-order multipolar neurons (FOMs) on which these bipolar

neurons synapse in the central nervous system, and the main functions for the trigeminal, ventrolateral placodal, and dorsolateral placodal cranial nerve components. This table is based predominantly on the human brain, as a representative of the mammalian condition, with the lateral line system included for the more general case across vertebrates. Some specialized receptive properties of the trigeminal nerve are included for perspective as well.

DORSAL CRANIAL NERVES: SENSORY COMPONENTS FOR GENERAL SOMATOSENSORY SENSATION

One of the most dramatic advances in the evolution of the head was the transformation of the first arch of the visceral skeleton into components of the jaws. Although the jaws continued to play a role in respiration by regulating the flow of oxygenated water to the gills, they also greatly altered the way that the animals fed and many aspects of their mode of living. Jawed fishes were able to become more active predators. The ability for predation had important consequences for subsequent evolutionary changes such as improved fins and tail propulsion for more rapid maneuvering to approach prey or to avoid predators, changes in body form to reduce drag, and camouflage to deceive prey or to deceive predators. The central nervous system evolved concurrently with these changes by providing the sensory input and motor control that made these behaviors possible.

TABLE 11-1. Classification, Neuron Locations, and Functions of the Trigeminal, Ventrolateral Placodal, and Dorsolateral Placodal Cranial Nerve Components

Nerve or Nerve Component	New Classification (Traditional ^a Classification)	Bipolar Neuron Location	First-Order Multipolar Location	Function
V Trigeminal	Somatic Afferent (GSA)	Trigeminal (Gasserian or semilunar) ganglion	Principal and descending nuclei of V	Face and oral cavity sensation and proprioception from jaw muscles; infrared reception; mechanoreception; electroreception; magnetoreception
VII _D Facial	Somatic Afferent (GSA)	Geniculate ganglion	Descending nucleus of V	External ear sensation and proprioception from facial muscles
VII _{VL} Facial	Ventrolateral Placodal Somatic Afferent (SVA)	Geniculate ganglion	Gustatory nucleus	Taste from anterior two thirds of tongue (ectodermally derived)
VIII and LL Vestibulocochlear and Lateral Line	Dorsolateral Placodal Somatic Afferent (SSA)	Cochlear (spiral), vestibular (Scarpa's), and lateral line ganglia	Cochlear, vestibular, and lateral line nuclei	Hearing, vestibular, and lateral line senses
IX _D Dorsal Glossopharyngeal	Somatic Afferent (GSA)	Superior (jugular) ganglion	Descending nucleus of V	Sensation from cutaneous area behind ear
	Visceral Afferent (GVA)	Inferior (petrosal) ganglion	Nucleus solitarius	Posterior tongue and throat sensation; carotid baroreceptors, osmoreceptors, chemoreceptors, etc.
IX _{VL} Ventrolateral Glossopharyngeal	Ventrolateral Placodal Visceral Afferent (SVA)	Inferior (petrosal) ganglion	Gustatory nucleus	Taste from posterior one third of tongue (endodermally derived)
X _D Dorsal Vagus	Somatic Afferent (GSA)	Superior (jugular) ganglion	Descending nucleus of V	External ear sensation, including tympanic membrane
	Visceral Afferent (GVA)	Inferior (nodose) ganglion	Nucleus solitarius	Sensations from thoracic and abdominal viscera
X _{VL} Ventrolateral Vagus	Ventrolateral Placodal Visceral Afferent (SVA)	Inferior (nodose) ganglion	Gustatory nucleus	Taste from epiglottis and throat region (endodermally derived)

^a GSA, General Somatic Afferent; GVA, General Visceral Afferent; SSA, Special Somatic Afferent; SVA, Special Visceral Afferent.

Somatosensory Innervation of the Head

The cranial nerve that is most closely associated with the development of the jaws is the trigeminal nerve (V). This nerve is derived from the nerve that supplies the first (mandibular) visceral arch (of the second head segment). Closely allied to the trigeminal nerve is the dorsal facial nerve (VII_D), which is derived from the nerve that supplies the second (hyoid) visceral arch (of the third head segment). These two nerves provide much of the sensory innervation from the skin and muscles of the head. These sensations include pain, temperature, touch, and proprioception.

The trigeminal nerve carries the sensory neurons from the jaws and elsewhere on the head as well as the motor neurons

that control the deep muscles of the head, that is, the jaw muscles. The dorsal facial nerve carries sensory neurons from the skin of the head and face as well as from the muscles in anamniotes, but in amniotes, relatively few of these somatosensory fibers are found in VII_D. The majority of the somatosensory fibers from the head enter the brainstem via the sensory roots of V. A few such fibers also enter the brainstem via IX_D and X_D.

The trigeminal system is best developed in animals with a prominent snout, such as alligators, birds, and other animals, such as pigs, in which the snout is used for exploration and manipulation. The presence of vibrissae (whiskers) on the snout is also associated with an expansion of the trigeminal system. Vibrissae are important for tactile exploration and to provide an indication that the snout is about to bump into

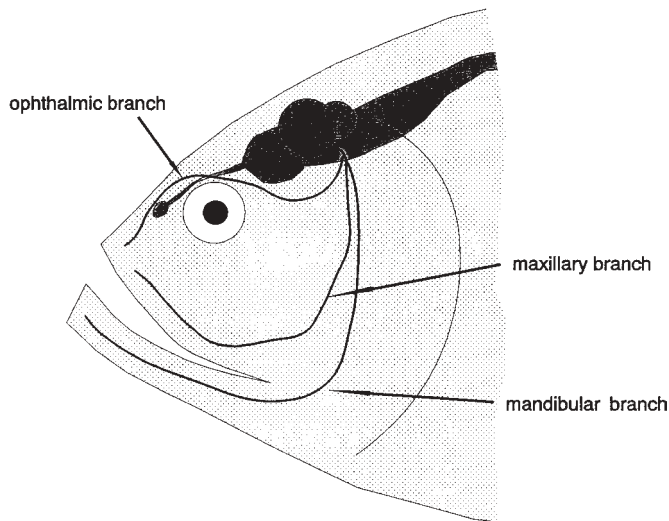


FIGURE 11-1. Distribution of the branches of the trigeminal nerve in a bony fish.

something. Many species of birds have a few rather untidy-looking feathers that stand out at the base of the bill. These feathers may be the avian equivalent of vibrissae and might possibly serve as air-speed indicators.

The trigeminal nerve has three great branches in mammals. The **ophthalmic branch** innervates the skin of the front part of the head region, the nonvisual parts of the eye including the muscles, and the snout. The **maxillary branch** innervates the upper jaw (the maxilla) including the upper teeth, the roof of the mouth, and the upper lip. The **mandibular branch** innervates structures of the lower jaw (mandible), including the lower teeth, the tongue, the floor of the mouth, and the lower lip.

Similar branches of the trigeminal nerve are present in nonmammalian vertebrates (Fig. 11-1), but in many of these groups, a separate profundus nerve has been identified that corresponds to the ophthalmic branch of the trigeminal nerve in mammals. The profundus nerve may represent the dorsal nerve of the first head segment (see Chapter 9). In *Latimeria*, the profundus nerve innervates the mucosal walls of a series of rostrally located tubes that contain the lateral line receptors. The profundus nerve probably carries pain and temperature information from the walls of the tubes. The lateral line receptors themselves are innervated by the anterodorsal lateral line nerve, which we will discuss below. Some other special adaptations of the trigeminal nerve, such as infrared (IR) detection in snakes, which we will discuss below, also involve the ophthalmic, or profundus, part of the trigeminal nerve.

Central Terminations of the Trigeminal Nerve

The central terminations (Fig. 11-2) of the axons of the trigeminal nerve are rather consistent in vertebrates. The fibers of the maxillary, mandibular, and ophthalmic branches that carry information about pain and temperature terminate in the **descending, or spinal, nucleus of the trigeminal nerve** (descending V) in the somatic afferent column, along with the

minor contribution of somatosensory axons entering from other cranial nerves (VII_D , IX_D , and X_D). Descending V is continuous at its caudal end with the dorsal horn of the spinal cord and appears to serve an equivalent function for the head. The sensory trigeminal axons from all three branches of the trigeminal nerve also terminate in the pons, in an expansion of the somatic afferent column called the **principal nucleus of the trigeminal** (principal V) (see Fig. 16-8), which receives information about position and fine touch. In both the principal V and descending V, the terminations of the axons remain segregated according to their source. In other words, a spatial map of the arrangement of structures in the head is maintained in the trigeminal nuclei.

The Mesencephalic Division of the Trigeminal System

An additional component of the trigeminal system remains to be described. This is the mesencephalic division, which is one of the most unusual components of any sensory system. It is a very consistent feature and can readily be identified in every class of vertebrates with the exception of lampreys and hagfishes. The unusual characteristic of this sensory nerve (the **mesencephalic tract, or root, of V**) is the location of its cell bodies, which are cholinergic and are known as the **mesencephalic nucleus of the trigeminal nerve**, or **mesencephalic V** [Fig. 11-2(A) and also see Fig. 16-8]. All nonvisual, sensory cranial nerves, with the exception of the mesencephalic root of V, have their cell bodies outside of the central nervous system in ganglia. These cell bodies are derived from neural crest and/or placodes. The cells that form mesencephalic V are likewise derived from neural crest and have the characteristic teardrop shape of pseudounipolar sensory neurons [Fig. 11-2(B-D)], but unlike other neural crest cells, they do not migrate ventrolaterally. Rather than being in a ganglion or close to the other cells and fibers of the trigeminal system, these cells lie in the dorsomedial part of the midbrain, in or adjacent to the tectal commissure, which is a broad band of axons that connects the right and left tectal hemispheres. This arrangement may be a remnant of an earlier stage in the evolution of the brainstem when such internal ganglion cells may have been more common.

Similar cells are seen in the spinal cord and/or medulla of many aquatic vertebrates. The latter are called **Rohon-Beard cells** and were discovered in lampreys by Ernst Reissner in the mid-1800s. It was Sigmund Freud, however, who, while still a medical student in the later part of that century, identified these cells as migrated spinal ganglion cells. In lampreys, these cells are present in the spinal cord and also along the entire extent of the medulla; they may be serially homologous to the mesencephalic V cells of jawed vertebrates.

The mesencephalic root of V carries proprioceptive information (for position sense) from the jaw muscles and the connective tissue surrounding the teeth. In mammals and amphibians, mesencephalic V also carries proprioception for the extraocular eye muscles, that is, the muscles that move the eyes. In contrast, in fishes and birds, the proprioceptors in the extraocular muscles are innervated by trigeminal axons that terminate in descending V. In sharks, the fibers of mesencephalic V do not respond to stimulation of muscle receptors; rather,

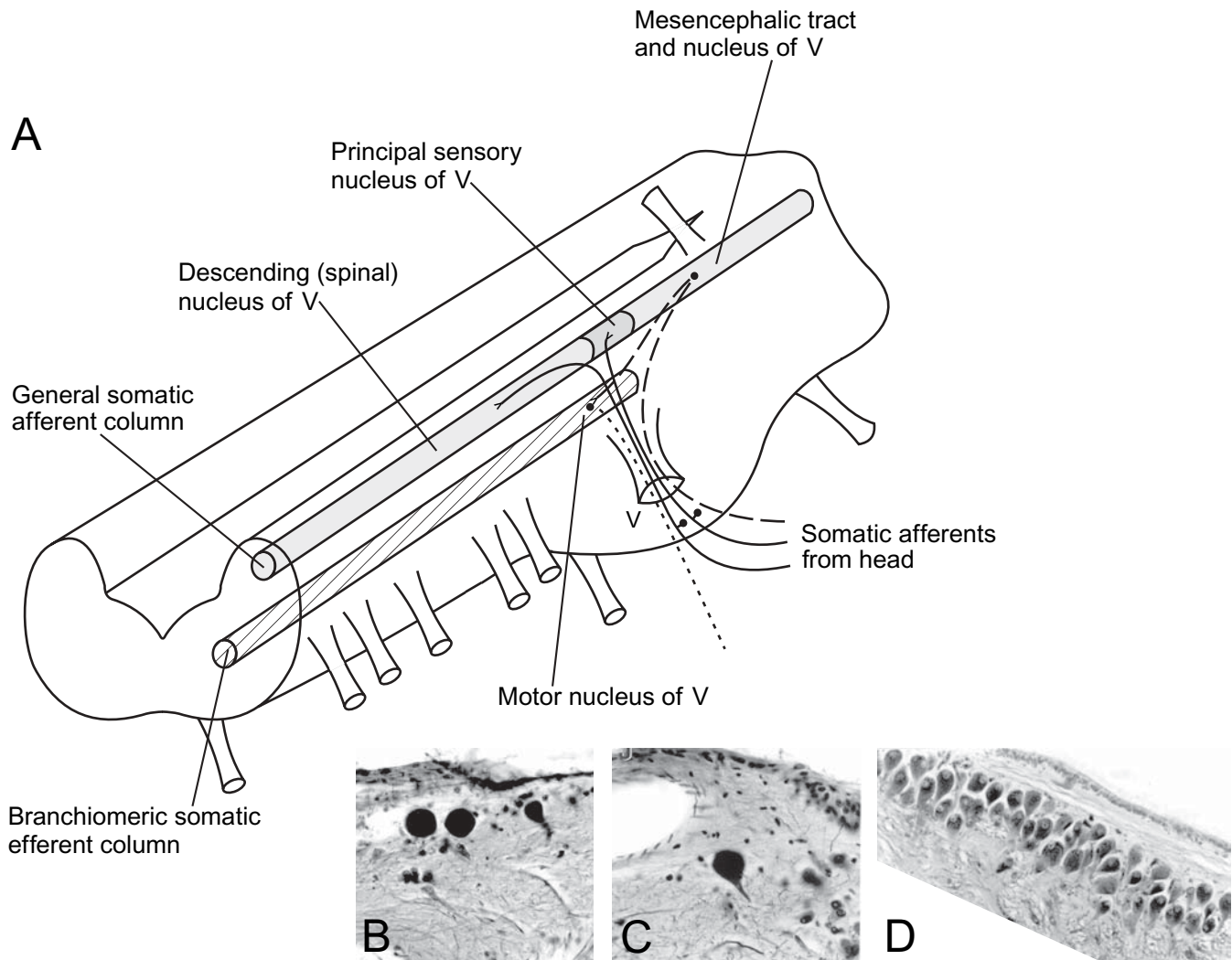


FIGURE 11-2. Schematic drawing (A) of the caudal brainstem, extracted from the template shown in Fig. 10-2. This version of the template represents the generalized vertebrate condition with regard to the trigeminal nerve, as shown here in a generalized mammal. Rostral is toward the right. The general somatic afferent cell column is shown with the terminations of the somatic afferents from the head via the trigeminal nerve. These afferent fibers end in the descending (spinal) and principal sensory nuclei of the trigeminal. The dendritic processes of cells of the mesencephalic nucleus of V also enter, and their axonal branches terminate on neurons in the motor nucleus of V, shown in the branchiomeric somatic efferent column. Photomicrographs of large, teardrop-shaped mesencephalic V cells in the herring *Clupea* (B) and the sunfish *Lepomis* (C) and of the unusually large mesencephalic V nucleus (at a lower magnification) in the tarpon *Elops* (D).

they respond to stimulation of the skin around the mouth and displacement movements of the teeth. The majority of the mesencephalic V fibers terminate in motor V (Fig. 11-2) and so would appear to play an important role in the regulation of jaw opening and closing and perhaps in the adjustment of jaw pressure.

Secondary Connections of the Trigeminal Nuclei

Most studies on the secondary connections of principal V and descending V have been done in mammals and birds. The

general organizational pattern of efferents from the trigeminal nuclei is that only the axons of the mesencephalic root of V terminate directly in the motor nucleus of V, which controls the contraction of the jaw muscles (see Chapter 12). In this case, a sensory neuron terminates directly on a motor neuron, forming a two-neuron (monosynaptic) reflex arc, which is the simplest type of neural network. In contrast, the efferents of principal V and descending V affect activity in motor V and motor VII_D indirectly by way of their terminations in the reticular formation, which in turn sends axons to the motor nuclei. The reticular formation often serves to coordinate the activity in related motor nuclei, such as motor V, motor VII_D, and the

three motor nuclei that control the eye muscles. Such coordination of jaw and eye muscles is important in feeding behaviors, especially in predatory animals.

Another secondary connection of the trigeminal system is a bundle of axons that ascends from descending V and principal V to a somatosensory nucleus in the dorsal thalamus. From the dorsal thalamus, axons pass up to the telencephalon and terminate in the somatosensory cortex or pallium. The somatotopic organization that exists in principal V and descending V persists throughout the entire pathway so that, at the level of the telencephalon, the cells that are responsive to stimula-

tion of various points on the head, snout, jaws, and mouth are arranged in separate groups.

An unusual variation on the general vertebrate pattern is found in birds, in which the target nucleus of principal V is not in the dorsal thalamus but in the telencephalon. This telencephalic cell group in birds is called **nucleus basorostralis**. It sends its efferents to a somatosensory telencephalic pallial area in a topographically organized fashion. Whether nucleus basorostralis is a homologue of the trigeminal, somatosensory, dorsal thalamic nucleus of mammals has not yet been resolved.

BOX 11-1. The Marvelously Versatile Trigeminal Nerve

The trigeminal nerve is exceptional in regard to the number of different types of peripheral receptors and modalities that it is capable of innervating and transmitting. In its most usual manifestation, the nerves end in either free nerve endings (for temperature and pain sensations) or as a variety of encapsulated and other specialized ending structures (for touch and position senses). In some cases, however, specializations have evolved that allow the trigeminal nerve to function for other modalities. These include infrared detection in some snakes, electro- and mechanoreception in monotremes, and magnetoreception in fishes, amphibians, and birds.

One of the remarkable adaptations of the trigeminal nerve—for infrared detection—has occurred in two families of snakes, as Peter Hartline and his co-workers found. In the boids (pythons and boa constrictors) and the crotalids or pit vipers (rattlesnakes, water mocassins, bushmasters, fer-de-lances, etc.), sensory pits are present on the head (Fig. 1). In the boids, the pits are principally on the lips; the pit vipers possess a prominent sensory pit below each eye. In both cases, the sensory pits are lined with photoreceptors that are sensitive not to the light that is visible to our eyes but to invisible infrared (IR) radiation.

IR radiation is emitted by all objects that have warmth and especially by mammals and birds, which maintain a high body temperature. Such warm bodies are easily detected by IR sensors in the absence of all visible light. One study of the rattlesnake's IR detection sense reported that the snake could detect a temperature difference of 0.003°C from the background, which is roughly the amount of heat radiated by a human hand at a distance of 0.5 meter. The IR detectors transmit their information to the brain via the maxillary branch of the trigeminal nerve. These neurons terminate in a special cell group, the **lateral trigeminal nucleus**, which is not found in non-IR detecting snakes. The nucleus is located lateral to descending V in the somatic afferent column. A similar, but independently evolved, lateral trigeminal nucleus has been reported in the vampire bat, which also detects IR radiation.

Recent physiological studies of the lateral trigeminal nucleus in rattlesnakes indicate that the neurons in this cell

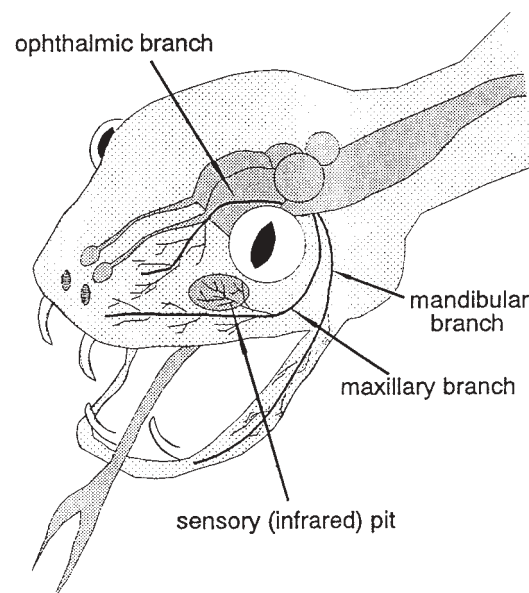


FIGURE 1. Distribution of the branches of the trigeminal nerve in a rattlesnake.

group possess many of the characteristics of cells in the visual system: small receptive fields and excitatory and inhibitory interactions that could serve to sharpen edges and provide a basis for the detection of motion and its direction. Of course, we have no idea what the rattlesnake's subjective experience of stimulation of its IR detectors is like, but the available evidence points to it being something very like vision.

In the crotalids, the lateral trigeminal nucleus sends its efferents to a special group of cells in the reticular formation, the **nucleus reticularis calor** (i.e., the reticular nucleus of warmth). This reticular nucleus sends its efferents to the tectum, which is the region of the midbrain in which various maps of the surrounding environment, such as visual and auditory, are processed. The efferents of the

BOX 11-1. The Marvelously Versatile Trigeminal Nerve—cont'd

boid lateral trigeminal nucleus project directly to the tectum. Tectal maps will be discussed in greater detail in Chapter 18.

Another quite remarkable adaptation has been found and studied in the platypus by Edmund Gregory and his co-workers and also by Paul Manger, Jack Pettigrew, and their co-workers. These monotreme (egg-laying) mammals have a prominent snout that resembles the bill of a duck. The “duckbill” of the platypus, rather than being keratinized as are bird bills, is leathery. Contained within the snout are rod-like structures that are mechanoreceptors and ampullary receptors similar to the electroreceptors of the lateral line system in aquatic anamniotes. These electroreceptors are capable of detecting the compound muscle-action potentials of the well-developed tail musculature of shrimp, on which platypuses feed. The receptors are innervated by the trigeminal nerve, and the mechano- and electrosensory inputs are relayed to the somatosensory cortex, which occupies a very large portion of the cerebral hemisphere. Most of this cortex is devoted to a representation of the duckbill. Thus, it appears that platypuses are highly focused on the input from the receptor system on their duckbills and depend on it to locate their prey. Similar mechano- and electroreceptive structures have been found on the beak of echidnas (spiny anteaters), a unique finding for a terrestrial animal.

A third specialized adaptation of the trigeminal nerve is for magnetoreception. This sensory capability is present in a wide range of animals, including both invertebrate and vertebrate taxa. Among the latter, Michael Walker has recently demonstrated that trout are magnetosensitive. The trigeminal nerve transmits the sensory input for this system from receptors located within the olfactory lamellae of the nasal cavity. The receptors are sensitive to tiny crystals of magnetite (Fe_3O_4). Walker has also proposed a vector summation model for homing pigeons that would utilize the magnetic total intensity to determine position. Matthew Williams and Martin Wild demonstrated sac-like structures located in the upper beak of the homing pigeon that are positive for iron and are innervated by the ophthalmic branch of the trigeminal nerve, and similar structures may be present in other species of migratory birds as well.

The work of Wolfgang and Roswitha Wiltshko and their co-workers has demonstrated magnetite-based magnetoreception in various birds as well as light-dependent magnetic compass orientation. A recent ultrastructural study from their laboratory has shown that the median ophthalmic nerve terminals themselves contain superparamagnetic magnetite and another inorganic iron compound (noncrystalline platelets of iron phosphate) that might allow detection of small changes of the geomagnetic field. The passerine birds that the Wiltshkos have tested, including European robins and garden warblers, require monochromatic light in the blue-green part of the spectrum for correct orientation to the magnetic field. This system thus con-

tributes to orientation and migratory abilities. Of course, it should be noted that magnetoreception and wavelength cues are not the only guides used by birds for navigation. They also employ visual cues in a highly cognitive manner, making use of landmarks, the position of the sun, and other information. For example, recent work in England has shown that homing pigeons use roads and other landmarks for determining their flight path. For more information on magnetoreception, see Box 18-1.

We would be remiss if we were to leave the subject of the trigeminal nerve without mentioning its arguably most important function—at least to those of us humans who appreciate hotly spiced food. The branches of the trigeminal nerve within the mouth are responsible for our appreciation of capsaicin ($\text{C}_{18}\text{H}_{27}\text{O}_3\text{N}$), the active substance of jalapeño and other hot peppers. The trigeminal nerve makes this unique contribution to our experience of taste and flavor. Chemosensitivity to capsaicin and other related stimuli that is mediated by the trigeminal nerve is not unique to the mouth, however. Solitary chemoreceptor cells are distributed across epithelial surfaces of the head and/or body in many vertebrates (see Box 2-2), and those on head surfaces are innervated by the trigeminal nerve. They may be present on the external skin or on internal surfaces, such as the nasal and/or olfactory epithelia. A unique system in hagfishes is similarly organized; this taxon has taste bud-like organs called Schreiner organs distributed over the entire epidermis and also on internal surfaces, including oral and related regions. They are innervated by a variety of spinal and cranial nerves, including the trigeminal nerve.

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BOX 11-I. The Marvelously Versatile Trigeminal Nerve—cont'd

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VENTROLATERAL PLACODAL CRANIAL NERVES: TASTE

Some of the earliest vertebrates, derived from ancestral chordates, were adapted to life as filter feeders in an aquatic environment, probably very much the way that larval lampreys and some jawed fishes survive today. These animals filter food particles or small prey from the water column that is pulled in by the suction action of the branchial muscles. The filtration is done by sticky mucus or by the gill rakers acting as a sieve. The trapped particles or prey are washed into the digestive tract, and the excess water is expelled along with respiratory gases. Some fishes are bottom feeders that suck up mouthfuls of bottom sediment, extract the edible morsels, and eject the

remainder, and some predatory fishes suck in mouthfuls of water that carry the prey into their mouths. All of these methods of feeding require mechanisms for differentiating between the edible and the inedible, between objects that produce illness and those that do not, and between more favored and less favored foods. These mechanisms are the chemical senses of gustation (taste) and olfaction (smell). In Chapter 11, we will discuss gustation. Olfaction, which is used not only for feeding but also for social recognition, orientation, territorial marking, and courtship, is a more complex subject and will be discussed in Chapter 29.

The receptors for gustation are taste cells located in groups on small peg-like projections known as **taste buds** (see Chapter 2). An animal's sensitivity to taste stimuli depends on the number of taste buds. The greater the number of taste buds, the higher is the probability that a stimulus molecule will be detected.

In fishes, taste buds are located not only in the mouth and in the throat but sometimes on the lips, on the surface of the head, and on the body skin. Many species of bony fishes have taste buds on the tips of their pectoral fins, which permit them to sample the taste qualities of the bottom sediment. The “whiskers” that give the catfish its name (technically known as **barbels**) are studded with as many as 20,000 taste buds and serve a similar, bottom-tasting function. In addition, the catfishes and the cyprinids, which include the common goldfish, have in excess of 150,000 taste buds all over their body surface. Although we find it difficult to imagine what this skin-tasting sense is like, it probably gives the fish a taste map of the surrounding environment, just as the electrosense gives certain fishes an electrical image of nearby objects and organisms and the IR sense provides an IR picture to certain snakes.

In tetrapods, all of which have tongues, the taste buds are located on the tongue as well as in the mouth and throat. Amphibians and reptiles have considerable numbers of taste buds, which suggests that their taste sensitivity is rather good. Birds, on the other hand, have relatively few taste buds compared with the other tetrapods and would appear to make less use of this sense.

The Gustatory System

The number of taste qualities that animals can detect is relatively few. The most commonly reported are sweet (sugars), salty (salts), sour (acids), and bitter (alkaloids). In addition, some taste neurons have been reported to be excited by certain amino acids, pure water, and monosodium glutamate (a taste called *umami*; see Chapter 2). Because human taste sensitivity is limited to sweet, sour, salty, bitter, and umami, we cannot imagine what amino acids or pure water taste like. Sensations in the mouth that are produced by chemical irritants, such as pepper and various “hot” spices and seasonings, are not transmitted either by the gustatory or by the olfactory nerves. These are somatic sensations just like pain and temperature and are carried by fibers of the maxillary and mandibular divisions of the trigeminal nerve (V) to the trigeminal nuclei in the somatic afferent column (see Box 11-1).

The Gustatory Nerves and the Nucleus Solitarius

The taste cells have no axons; instead, axons of gustatory fibers of the ventrolateral facial (VII_{VL}), ventrolateral glossopharyngeal (IX_{VL}), and ventrolateral vagus (X_{VL}) nerves detect changes in excited taste cells and transmit this information to the common target of taste axons no matter by which nerve they enter the brain: the gustatory nucleus (a rostral division of nucleus solitarius), which is at the rostral end of the visceral afferent column of the medulla (Fig. 11-3).

The nucleus solitarius consists of two divisions, with their boundary being roughly at the level of the entrance of the vagus nerve. The rostral division of the nucleus solitarius is the region that receives the gustatory fibers from VII_{VL}, IX_{VL}, and X_{VL} and is now recognized as a separate nucleus—the gustatory nucleus. This is a ventrolateral, epibranchial placodal afferent system rather than a “special” afferent system as previously believed. Some taste buds are derived from ectoderm, while

others are derived from endoderm, so the gustatory fibers are most properly classified as either somatic or visceral, respectively, depending on the embryonic origin of the taste buds that they innervate. In tetrapods, the endothelial lining of the rostral two thirds of the fleshy tongue is derived from ectoderm. The fibers of VII_{VL} that innervate these ectodermally derived taste buds are thus somatic afferent fibers. In those fishes that have ectodermally derived taste buds on the external body surface, their innervation is also by VII_{VL}, via a recurrent branch of this nerve, as discussed further below. In contrast, the fibers of IX_{VL} and X_{VL} that innervate the more caudally lying, endodermally derived taste buds of the tongue and oral cavity are visceral afferent fibers.

The caudal division of nucleus solitarius is the general visceral component of the visceral afferent column and receives fibers via the dorsal glossopharyngeal (IX_D) and the dorsal vagus (X_D) nerves (shown previously in Fig. 10-3) from the throat region and the viscera of the body, such as the digestive, circulatory, and respiratory systems. Although not involved in the perception of taste, the latter afferents of IX_D and X_D carry input that, along with taste afferents, affects feeding behavior.

A somatotopic organization exists in the gustatory nucleus such that the gustatory nerves from the different regions of the head (and the body in those animals with skin taste buds) enter the nucleus in approximately the same order as they are located in the body, that is, axons from more rostral regions of the mouth (or body) enter the more rostral portions of the gustatory nucleus. A similar, topographic arrangement has been found in the terminations of axons from the general viscera in the caudal division of nucleus solitarius. Axons from the various internal organs terminate in the caudal nucleus solitarius in the same order as the organs are arranged in the body.

Secondary Connections of the Gustatory Nucleus and Nucleus Solitarius

The pathways taken by efferent axons from the gustatory nucleus and the caudal division of nucleus solitarius have been studied in some detail in mammals, especially rodents and primates. In primates, the efferents of the gustatory nucleus follow the typical routes of the sensory systems of cranial nerves that terminate in the lower brainstem. From the gustatory nucleus, ascending fibers project to a nucleus in the dorsal thalamus, which in turn projects to the telencephalon. The gustatory part of the dorsal thalamus is situated close to the nucleus that receives somatosensory input. The dorsal thalamic gustatory nucleus projects to one or more regions of the telencephalon—gustatory neocortex and areas in the ventral part of the telencephalon. As in the dorsal thalamus, the telencephalic gustatory cells are not far from the somatosensory cells.

An additional nucleus in this system is the **parabrachial nucleus**, which is located in the dorsal pons. The medial part of this nucleus receives projections from the gustatory nucleus and is sometimes referred to as the **pontine taste area** (PTA). It contains a topographic representation of the gustatory receptors on the tongue. The gustatory part of the parabrachial nucleus serves as an intermediary between the gustatory nucleus and the gustatory dorsal thalamus and also projects to the hypothalamus and amygdala. The main gustatory pathways

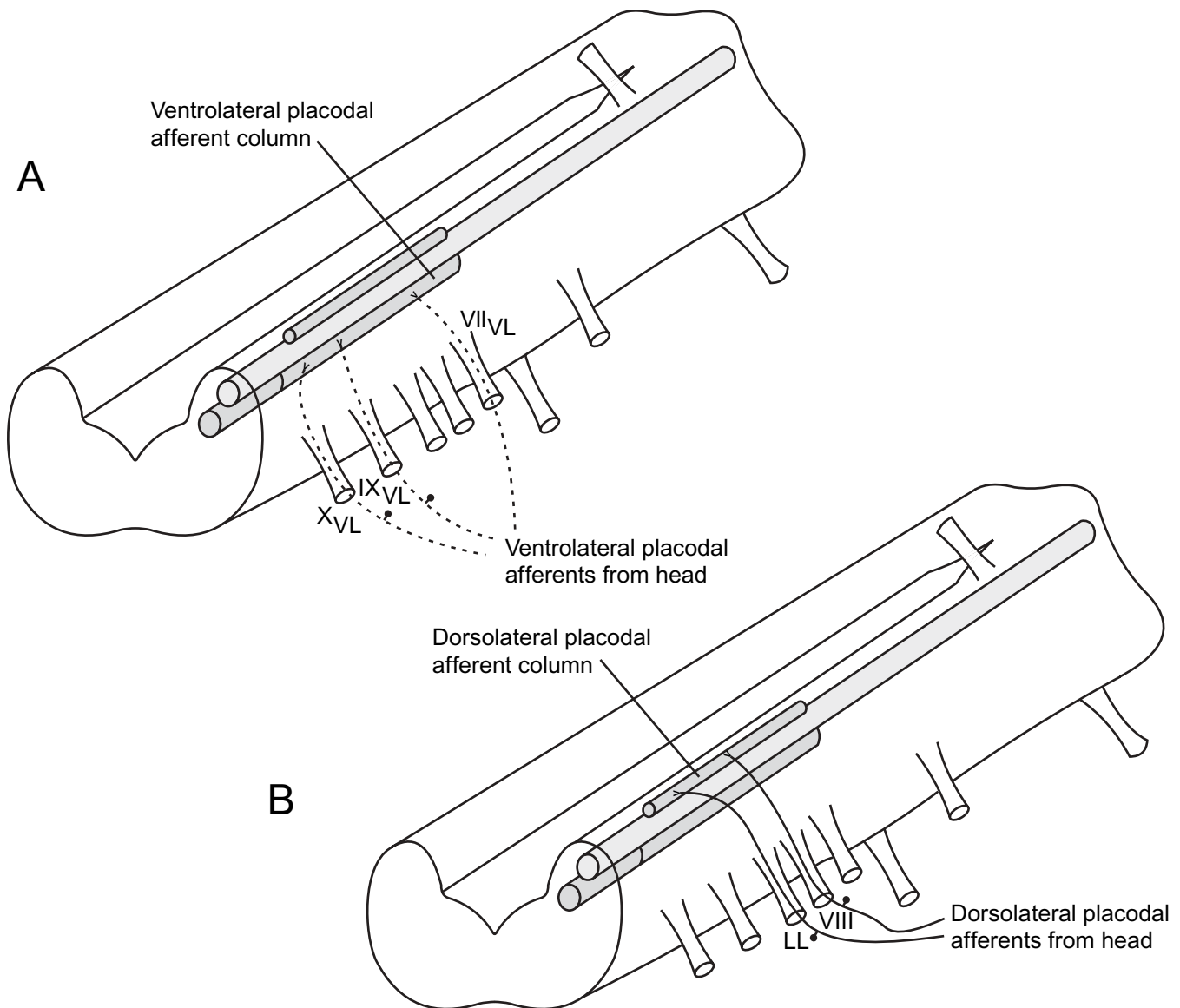


FIGURE 11-3. Schematic drawing of the caudal brainstem, extracted from the template shown in Fig. 10-2 but adapted here to represent a generalized aquatic vertebrate. A: ventrolateral placodal afferent cell column is shown with the terminations of the afferents from the head that carry taste sensations via the dorsal facial, dorsal glossopharyngeal, and dorsal vagus nerves. These afferent fibers end in the gustatory nucleus within the rostral part of this column. B: dorsolateral placodal afferent cell column is shown with the vestibulocochlear and lateral line afferents that enter the brainstem via cranial nerve VIII and the lateral line nerves, respectively. Most aquatic vertebrates have six lateral line nerves, only one of which is represented here for simplicity.

through the thalamus to the neocortex are shown in Figure 11-4.

The cells of the caudal, visceral division of nucleus solitarius send some of their axons to the dorsal motor nucleus of the dorsal vagus (X_D) nerve. This nucleus, which is part of the visceral motor column, is the source of parasympathetic axons that distribute to the viscera of the thorax (chest) and abdomen and other brainstem motor nuclei that control salivation.

Nucleus solitarius also projects to a more ventral nucleus in the brainstem called **nucleus ambiguus**. There is probably a stronger input to nucleus ambiguus from the gustatory nucleus than from the more caudal, viscally related nucleus solitarius. As discussed in Chapter 12, nucleus ambiguus gives rise to branchiomeric somatic efferent axons in the dorsal glossopharyngeal, dorsal vagus, and accessory nerves that innervate the muscles of the pharynx (throat).

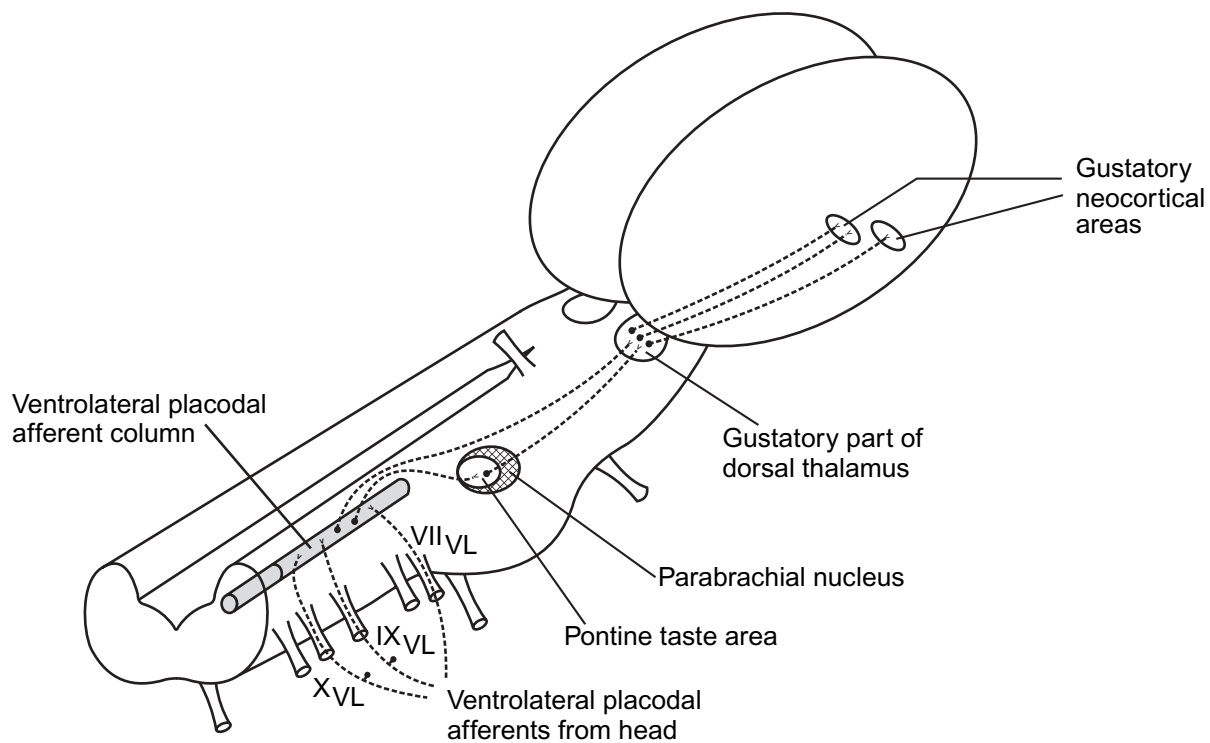


FIGURE 11-4. Main ascending gustatory pathways via the dorsal thalamus to the neocortex in mammals. The gustatory system also projects to the hypothalamus and amygdala.

Cyprinid and Silurid Gustatory Specializations

Although taste is very well developed in fishes in general, two suborders of ray-finned fishes have become highly specialized for the use of the gustatory sense; these are the cyprinids, which include the carps, minnows, chubs, and goldfishes, and the silurids (or catfishes). As we discussed previously, these animals not only have mouth, throat, and skin taste buds, as do other species of fishes, but they have evolved a vast system of taste receptors over virtually the entire body surface. Along with this expansive gustatory surface, a system of elaborately organized central structures has developed that rivals the most complex neural organizations seen in any central nervous system.

Both groups of fishes are bottom feeders, and the mechanisms that they have evolved are highly sophisticated adaptations for the separation of food particles from inedible bottom sediment. In goldfishes, for example, two opposing surfaces in the oropharynx (mouth and throat) manipulate bottom sediment in such a way as to separate the edible and tasty particles from those that are inedible or unpalatable. These surfaces are the **palatal organ**, which is a muscular structure attached to the roof of the mouth, and the surface of the gill arches. Both of these structures are studded with thousands of taste buds, which are innervated by branches of the ventrolateral vagus (X_{VL}) nerve. The gustatory branches of X_{VL} terminate in the gustatory nucleus, just as in other vertebrates, but what is so unusual in cyprinids and silurids is that the gustatory nuclei of the right and left sides have “ballooned” out to form rather prominent lobes on the caudal brainstem. They are known as

the **vagal lobes** [more properly, the glossopharyngeal-vagal lobes because the axons of the ventrolateral glossopharyngeal (IX_{VL}) nerve also terminate in their rostral ends]. The internal structure of the vagal lobes consists of a series of nine layers of neurons with a complex organization. In addition to a topographical organization of mouth structures in the vagal lobe, taste axons from each of the specialized structures terminate in specific layers. For example, axons innervating the taste buds of the palatal organ project to layer six; those innervating the taste buds on the gill arches project to layers two and four; layer nine receives both palatal and gill arch axons. The general visceral afferent axons from IX_D and X_D terminate in a separate, visceral afferent nucleus.

In addition to the paired vagal lobes, these fishes have a second pair of lobes, called the **facial lobes**, which lie rostral-medial to the vagal lobes. As the name implies, the facial lobe receives the gustatory axons of the ventrolateral facial (VII_{VL}) nerve. In catfishes, this nerve is quite elaborate with branches from the upper lip, the lower lip, the anterior palate, the pectoral fin, which is also used for bottom tasting, and a branch known as the recurrent branch because it “runs back” toward the tail. The recurrent branch serves the vast number of taste buds on the body surface. A topographical organization is found in the facial lobe with the more rostral structures being represented in the rostral portion of the lobe. The vagal and facial lobes and their relationship to the trigeminal system are shown in Figure 11-5.

Some of the efferents of the vagal and facial lobes are involved in the coordination of various feeding and postural reflexes. The vagal lobe projects to those general somatic effer-

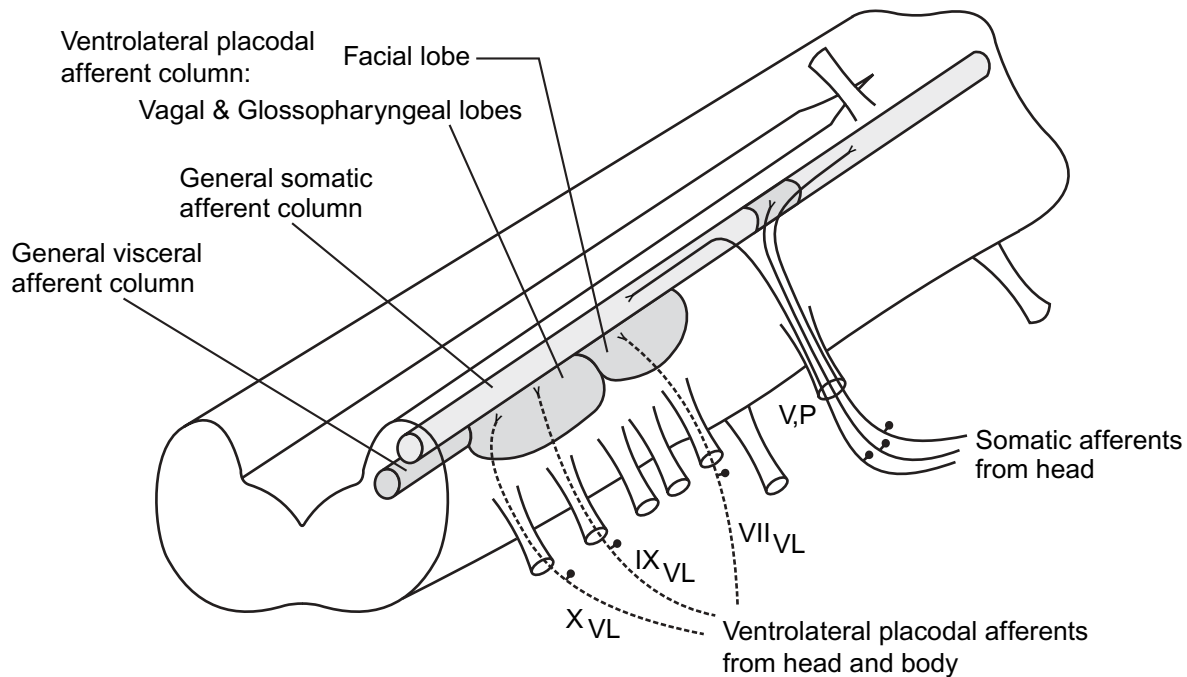


FIGURE 11-5. General somatic afferents from the head to the general somatic afferent column and ventrolateral placodal (gustatory) afferents to the facial, glossopharyngeal, and vagal lobes in cyprinids and silurids.

ent motor nuclei of the caudal brainstem that control the palatal organ and other muscles of the oropharynx. The facial lobe projects to a nucleus located near the border of the medulla and spinal cord, called the **spinotrigeminal funicular nucleus**, which provides a point of interaction between gustatory information and tactile information from the head and the body.

The major efferent projections of the facial and vagal lobes of goldfishes (Fig. 11-6) are ascending and are kept segregated through the relays in the pathway. Both lobes project to a nucleus located in the pons called the **superior secondary gustatory nucleus**. The vagal lobe projects to its lateral part, while the facial lobe projects to its medial part. The superior secondary gustatory nucleus relays its vagal lobe input to a structure called the **torus lateralis** (see Chapter 17), which is located along the lateral aspect of the midbrain, while its facial lobe input is relayed to the **inferior lobe of the hypothalamus**. The superior secondary gustatory nucleus also projects to a **tertiary gustatory nucleus** in the caudal part of the diencephalon, which is a component of the **preglomerular nuclear complex** (see Chapter 20) and likewise relays its vagal and facial lobe inputs to the torus lateralis and inferior lobe of the hypothalamus, respectively. The latter structure and the torus lateralis are also reciprocally connected with each other, and they both project to another component of the preglomerular nuclear complex called the **posterior thalamic nucleus**, which in turn projects to the telencephalic pallium (see Chapter 25). The superior secondary gustatory nucleus appears to be the homologue of the gustatory portion of the parabrachial nucleus, that is, the pontine taste area, of mammals. The inferior lobe of the hypothalamus may be com-

parable functionally (i.e., analogous) to the lateral hypothalamus of mammals, since both are involved in feeding behaviors.

The ascending gustatory pathways are not identical between cyprinids, as exemplified by the goldfish, and silurids, however. In silurids, the vagal and facial lobe give rise to similar ascending projections to the secondary gustatory nucleus, which in turn projects to a number of diencephalic sites, including the inferior lobe of the hypothalamus and the medial part of the preglomerular nuclear complex. In contrast to cyprinids, the major gustatory relay to the telencephalon arises directly from the inferior lobe of the hypothalamus itself, rather than passing through another nuclear relay in the preglomerular/posterior diencephalic region. Likewise, some variation in the ascending gustatory pathways occurs in other teleosts. For example, in a cichlid fish, the tertiary gustatory nucleus of the preglomerular nuclear complex is the main source of the projection to the telencephalic pallium, which terminates within its dorsomedial part, Dm, and the secondary gustatory nucleus also projects directly to the pallium, terminating in its posterior part, Dp.

In summary, we can see that the sense of taste has been developed to a superb degree in the cyprinids and silurids. At the peripheral end, the distribution of receptors on the body surface, fins, lips, and in the mouth provides the animal with a highly detailed taste map of the environment as well as the means for detecting food items and rejecting inedible or noxious objects. These processes are made possible by an extraordinary group of central structures—complex lobes with individual layers that receive very specific inputs and are organized topographically. The extreme development of the vagal lobe/facial lobe complex in these fishes is an excellent illus-

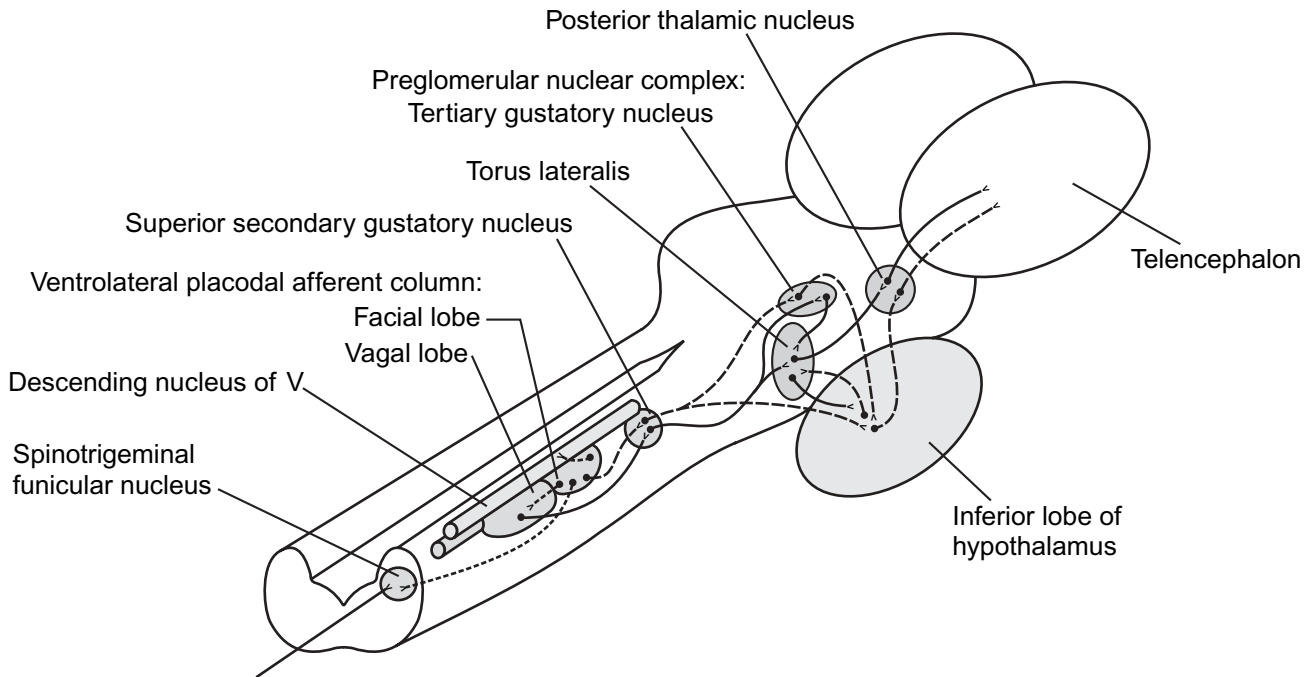


FIGURE 11-6. Ascending gustatory pathways in the goldfish, a cyprinid, including the gustatory input to the hypothalamus. Only some of the connections of the various nuclei are shown here. The short-dashed lines indicate local or descending projections from the facial lobe, the long-dashed lines indicate the ascending facial lobe pathway system, and the solid lines indicate the ascending vagal lobe pathway system. Pathways partly based on Rink and Wullmann (1998).

tration of one of the ways that the nervous system responds to adaptive pressures for the increased use of a neural system.

A great deal of effort has been expended to work out the details of the vagal lobe/facial lobe system in cyprinids and silurids. We have good reason to believe that this research will greatly enhance our understanding of the way taste information (and other sensory information as well) is processed in the central nervous system of all vertebrates. One way to understand a biological system is to study it in an animal that is specialized for its use.

DORSOLATERAL CRANIAL NERVES: LATERAL LINE AND OCTAVAL SYSTEMS

In aquatic vertebrates, the dorsolateral series of placodes gives rise to multiple nerves that fall into as many as four main sensory categories:

- Mechanosensory lateral line.
- Electrosensory lateral line.
- Auditory.
- Vestibular sense.

In terrestrial vertebrates, the lateral line system is absent, and only the senses associated with the eighth nerve, that is, the auditory and vestibular senses, develop.

In the aquatic environment, the visual, auditory, and chemosensory systems aid in the detection of the presence of other animals. The lateral line system is an additional important detector of other animals. It functions over a greater range of environmental conditions than the other sensory systems—in calm, clear, illuminated water as well as in turbid, murky water and in darkness. The lateral line sensory system has two major components in many vertebrates: a mechanosensory system and an electrosensory system.

The mechanosensory lateral line allows an aquatic animal to perceive other moving animals at a distance. Current-like movements of the water caused by the motion of other animals (predators, prey, conspecific sexual partners, or other members in a school) are detected by the lateral line neuromasts and/or pit organs (see Chapter 2), the mechanosensory receptors. Behavioral studies have shown that such detections are responded to and are thus important to the animal. On the other hand, water displacements caused by the animal's own movements can be detected by the mechanoreceptors, but reactions to these stimuli are suppressed by other neural mechanisms. Motor control and related feedback mechanisms, rather than the lateral line, are used to regulate locomotory behavior.

The electrosensory lateral line is used for a wide range of functions. It is often used to detect and identify prey, whether the prey is another free-swimming animal or an animal concealed on the bottom under a layer of sand or mud. The electrical profile of such animals can be located and identified by the ampullary or tuberous receptors (see Chapter 2) of the lateral line electrosensory system. In the variety of fishes that

can produce electrical signals—an electric organ discharge, or **EOD**—the electrosensory system plays an important role in social interactions, including the recognition of individual conspecifics within a social hierarchy.

The auditory and vestibular senses are common to aquatic and terrestrial vertebrates. Auditory receptors respond to pressure waves with accompanying particle motion, that is, to sound. The frequency of the waves and the location of their source are analyzed within the auditory system. Vestibular receptors are involved in maintaining equilibrium and respond to gravitational and other accelerational cues that allow for orientation of the body within the three spatial dimensions.

The Lateral Line System

The mechanosensory lateral line system is widely distributed in aquatic anamniotes. It was apparently present in the earliest vertebrates, as it has been identified in agnathans, cartilaginous fishes, bony fishes, lungfishes, the crossopterygian *Latimeria*, and aquatic amphibians. The mechanosensory lateral line system is thus a ubiquitous feature of anamniote vertebrates, and its evolutionary history is more conservative than that of electroreceptive lateral line systems.

An electroreceptive lateral line system has been evolved independently at least several times. Electroreception appears to have been evolved in the ancestral vertebrate stock of at least lampreys and jawed vertebrates, since morphologically similar electroreceptive systems are known to be present in lampreys, cartilaginous fishes, lungfishes, the crossopterygian *Latimeria*, and many amphibians. Among nonteleost bony fishes, a similar electroreceptive system is present in reedfishes and sturgeons. Electroreception appears to have been lost in the common ancestral stock of the Holostei (gars and the bowfin) and the Teleostei, however. It was then reevolved independently three or four times. These convergent electroreceptive systems are present in two different groups of ostariophysans, silurids and gymnotids, and in two different groups of osteoglossiforms, the mormyrids and notoapterids. (The electromotor communication systems of mormyrids and gymnotids are discussed in Chapter 12.)

The receptors for the mechanosensory lateral line usually lie within canals that are arrayed over the surface of the head and body. Figure 11-7 shows the distribution of the mechanosensory lateral line canals on the head of the coelacanth *Latimeria*, as well as the so-called rostral organ that contains electroreceptors in this species. The mechanoreceptors and electroreceptors are innervated by up to six separate nerves, the **anterodorsal, anteroventral, otic, middle, supratemporal, and posterior lateral line nerves**. Not all vertebrates with the lateral line system have all six nerves. The urodele amphibian *Ambystoma*, for example, has five lateral line nerves (Fig. 11-8), lacking an otic lateral line nerve.

An interesting specialization of the mechanosensory lateral line system in cartilaginous fishes is the innervation of the spiracular organ, which is a specialized receptor apparatus associated with the spiracular gill slit. Typical sensory hair cells are contained in a large neuromast that lines the spiracular pouch. These cells are innervated by a branch of the anterior lateral line nerve, which projects to octaval nuclei, the vestibulocerebellum, and, unusually, directly to part of the reticular

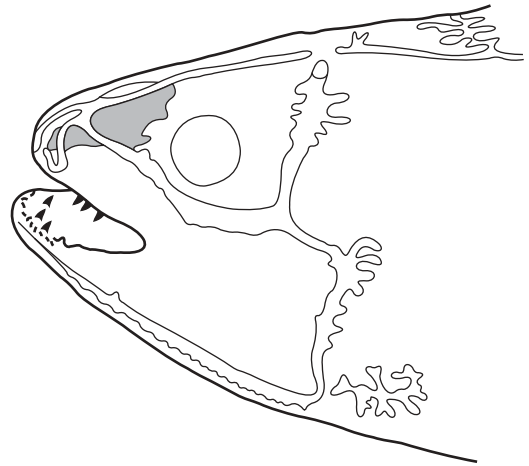


FIGURE 11-7. Drawing of the mechanoreceptive lateral line canals and the putative electroreceptive rostral organ (gray shading) in the coelacanth *Latimeria*. Rostral is toward the left. Adapted from Northcutt (1986) and used with permission of John Wiley & Sons.

formation. The spiracular organ is sensitive to flexor movements of the hyomandibula-cranial joint.

In the medulla, the mechanoreceptive lateral line fibers terminate primarily in two structures (Fig. 11-9), the **eminentia granularis** of the cerebellum and part of the **lateralis column**. In bony fishes, the lateral column consists of a large nucleus that forms most of the column's rostrocaudal extent, called **nucleus medialis** or **nucleus intermedius**. The more caudal nucleus in the column, **nucleus caudalis**, also receives mechanosensory input. In cartilaginous fishes, the mechanoreceptive cell group is similarly called the medial (or intermediate) octavolateralis nucleus, and in amphibians, it is called nucleus intermedius.

The position of the column of nuclei that receive mechanoreceptive lateral line inputs is relative to one or two other cell columns present in the medulla. The mechanoreceptive nuclei generally lie dorsal and/or lateral to a cell column, the octaval column, which receives input from the eighth nerve [Fig. 11-10(A)]. In electroreceptive nonteleost bony fishes, the mechanoreceptive lateral line column additionally lies lateral or ventrolateral to the cell column that receives the electrosensory lateral line input [Fig. 11-10(B)], called **nucleus dorsalis**, while in electroreceptive teleosts, the mechanoreceptive lateral line column is medial or ventromedial to the electroreceptive area, called the **electrosensory lateral line lobe** (Fig. 11-11). In cartilaginous fishes, this cell column is called the **dorsal octavolateralis nucleus**. In electroreceptive amphibians, the mechanosensory nucleus intermedius lies ventral to the electrosensory column, which is called nucleus dorsalis.

The ascending projections that arise from both the mechanosensory and electrosensory lateral line nuclei travel with octaval fibers in the **lateral lemniscus**. This pathway is bilateral but projects predominantly to the contralateral side. The lateral lemniscus terminates in a part of the roof of the midbrain called the **torus semicircularis** in most anamniotes but is referred to as the **lateral mesencephalic nucleus** in

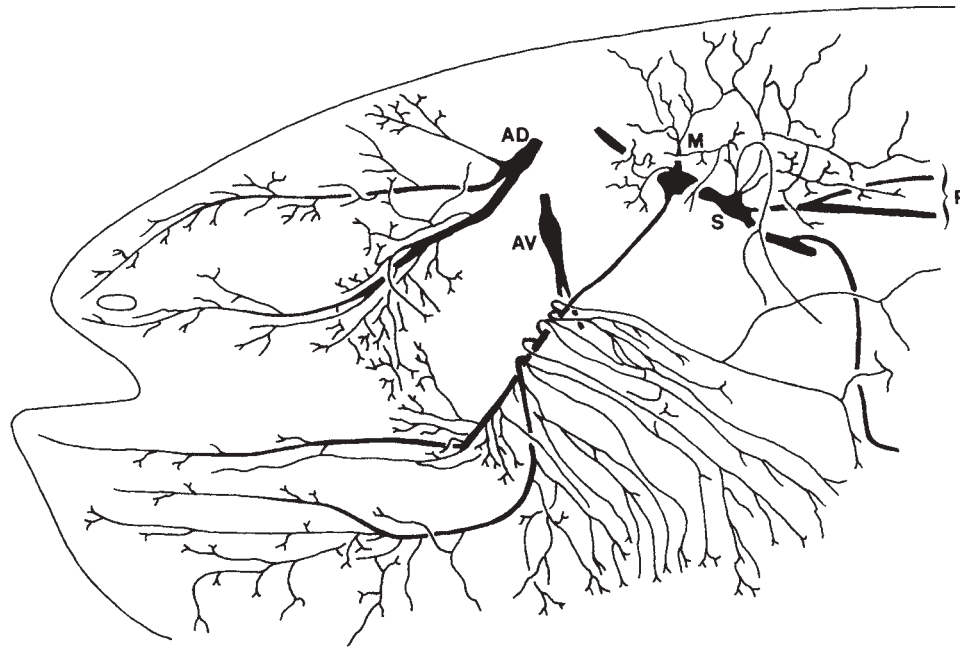


FIGURE 11-8. Drawing of the major branches of the five lateral line nerves present in the axolotl, *Ambystoma mexicanum*, which lacks an otic lateral line ramus. Rostral is toward the left. Abbreviations: AD, anterodorsal lateral line nerve; AV, anteroventral lateral line nerve; M, middle lateral line nerve; P, posterior lateral line nerve; S, supratemporal lateral line nerve. Adapted from Northcutt (1992) and used with permission of John Wiley & Sons.

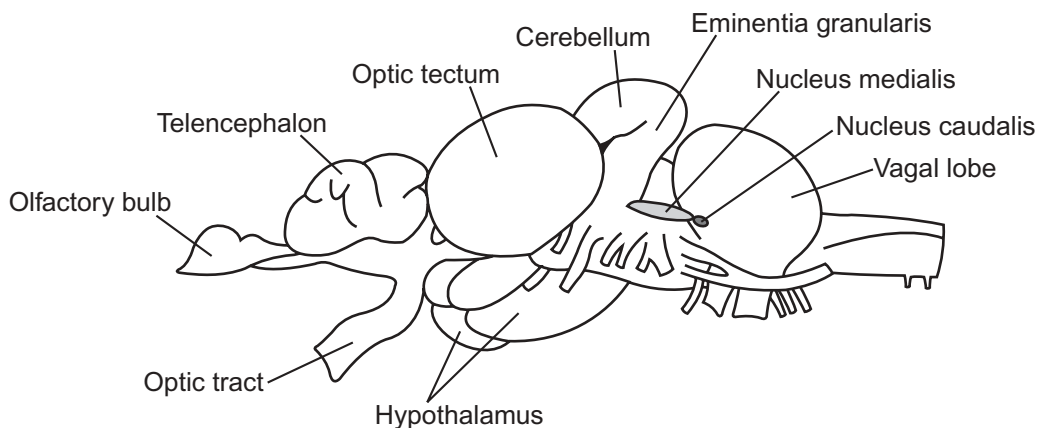


FIGURE 11-9. Lateral view of the brain of a goldfish (*Carassius auratus*) with the position of the lateralis column projected onto it. Adapted from Puzdrowski (1989) and used with permission of S. Karger AG, Basel.

some sharks and as a group of several nuclei—the **lateral mesencephalic complex**—in other sharks. Within the midbrain roof, the zones of termination of the mechanosensory, electrosensory, and octaval fibers remain separate (see Fig. 11-13). Within each of the lateral line sensory systems, a spatial map of the input is also maintained. From the midbrain, lateral line input is relayed through the **preglomerular nuclear complex** in the caudal diencephalon in bony fishes (see Chapter 20), or its putative homologue in cartilaginous fishes, to the telencephalon.

The Octaval System

The octaval system consists of the auditory and vestibular rami of the eighth cranial nerve and their central structures and connections. These two rami are present in all vertebrate groups, but substantial evidence exists showing that at least part of the peripheral auditory receptor apparatus has been independently evolved in fishes and among tetrapods. Similarities in the central nervous parts of these systems allow for the possibility that at least some of the auditory nuclei and path-

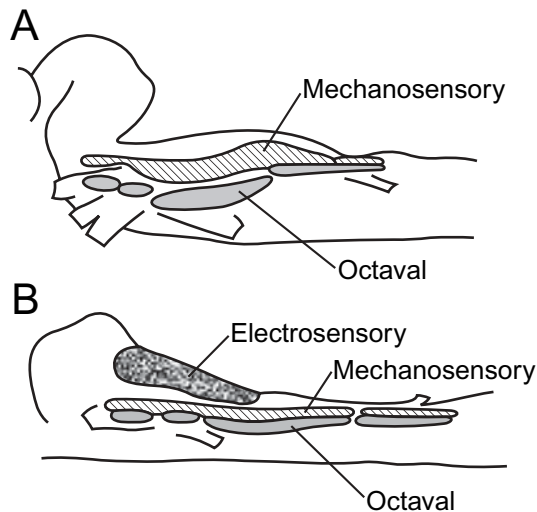


FIGURE 11-10. Projection onto a lateral view of the brainstem of nuclei receiving (A) mechanosensory (diagonal lines) and octaval (gray fill) projections in the bowfin (*Amia*) and (B) electrosensory (random stippling), mechanosensory (diagonal lines), and octaval (gray fill) projections in a sturgeon (*Scaphirhynchus*). Adapted from McCormick (1989) and used with kind permission of Springer Science and Business Media.

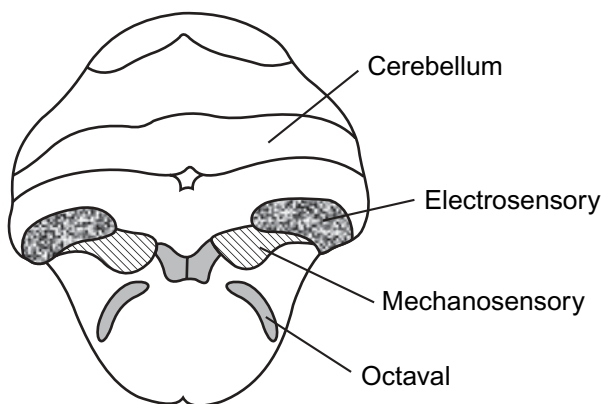


FIGURE 11-11. Drawing of a transverse section through the brainstem of the osteoglossomorph fish *Xenomystus* showing the relative positions of the electrosensory (random stippling), mechanosensory (diagonal lines), and octaval (gray fill) nuclei. Adapted from McCormick (1989) and used with kind permission of Springer Science and Business Media.

ways were maintained through periods of change in the peripheral receptor apparatus. Thus, some of the octaval nuclei may be homologous among the various groups of vertebrates, particularly at midbrain and more rostral levels, but some of the relationships of the various medullary octaval nuclei in different vertebrate groups remain open to question.

In most vertebrates, vestibular and auditory fibers terminate within various parts of the brainstem, including the cerebellum, reticular formation, and the **octaval column** in the medulla. The octaval column is the main auditory region involved in relaying the input to more rostral parts of the brain. Where a lateral line system is also present, the octaval column lies ventral to it, as noted above.

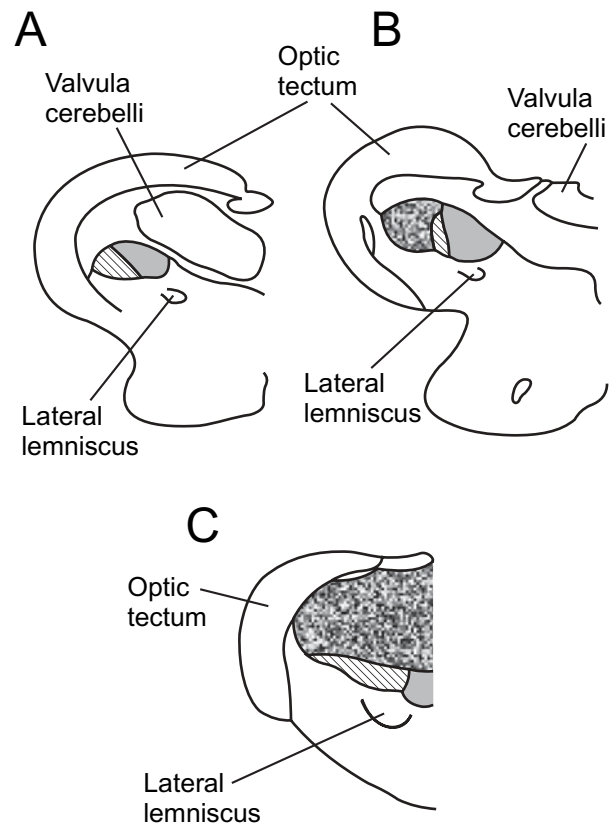


FIGURE 11-12. Drawings of transverse hemisections through the brainstem in three ostariophysan fishes: (A) *Cyprinus*, (B) *Ictalurus*, and (C) *Eigenmannia*. The areas of termination of ascending projections in the torus semicircularis are shown for electrosensory (random stippling, as in Figs. 11-10 and 11-11), mechanosensory (diagonal lines), and octaval (gray fill) pathways. Adapted from McCormick (1989) and used with kind permission of Springer Science and Business Media.

In lampreys and hagfishes, the eighth nerve terminates within the octaval column but not in any other brainstem sites. In lampreys, the octaval column has three nuclei, two of which, the **ventral** and **octavomotor** nuclei, receive the bulk of the eighth nerve fibers. In hagfishes, the eighth cranial nerve projections are primarily confined to a single area, called the **ventral nucleus of the area acusticolateralis**.

In both jawless and jawed fishes, at least some of the octaval endorgans are thought to process both auditory and vestibular information. In bony fishes, the nerves from all of the octaval endorgans primarily terminate within the octaval column, which comprises at least four nuclei, the **anterior**, **magnocellular**, **descending**, and **posterior nuclei** (Fig. 11-10). Auditory input that is relayed through the octaval column to more rostral levels is primarily routed through the dorsal parts of the anterior and descending nuclei. Auditory input is relayed to the roof of the midbrain—the torus semicircularis in most anamniotes and the lateral mesencephalic nucleus or complex in cartilaginous fishes. The fibers ascend via the lateral lemniscus in a primarily contralateral pathway, as do the lateral line projections (Fig. 11-12). Just as a spatial map is maintained in the lateral line system, a tonotopic representation is main-

tained in the auditory pathway. In bony fishes, an auditory pathway from the midbrain to the diencephalon (preglomerular nuclear complex), and thence to the telencephalon, has been traced. Auditory responses have been recorded in the telencephalon of sharks, although the anatomy of the ascending pathway remains to be studied.

In amphibians, two patterns of octaval nuclei exist in the medulla. One of these patterns is seen in nonanuran amphibians, in which an octaval column is present ventral to the lateral line sensory zone. This column can be divided into three nuclei that correspond to the anterior, magnocellular, and descending nuclei of fishes. The dorsal parts of these nuclei primarily receive auditory input, while the ventral parts primarily receive vestibular input.

The second pattern is present in anurans. In most adult anurans, the mechanosensory lateral line system is absent, and two columns in receipt of octaval input are present. The dorsal column contains one nucleus, the **dorsolateral nucleus**, which receives auditory input. The ventral column contains up to four nuclei: the **anterior**, **lateral octaval**, **medial vestibular**, and **caudal nuclei**. Auditory inputs are primarily confined to the dorsal parts of these nuclei and vestibular inputs to their ventral parts. The dorsolateral nucleus is the main nucleus for relay of auditory information to more rostral parts of the brain. The most prominent rostral projection is via the lateral lemniscus directly to the torus semicircularis and thence, via the dorsal thalamus, to the telencephalon. Pathways that relay auditory information to the torus semicircularis through secondary medullary nuclei, particularly a nucleus called the **superior olivary nucleus**, are also present.

In nonmammalian amniotes, the cochlear nerve terminates primarily in two medullary nuclei, a laterally lying **nucleus angularis** and a medially lying **nucleus magnocellularis**. Nucleus magnocellularis projects bilaterally to the **nucleus laminaris** (Figs. 11-13 and 11-14), which is a third nucleus that lies between the two cochlear receptive nuclei.

Nuclei angularis and laminaris give rise to bilateral pathways that project directly to the roof of the midbrain and also indirectly to it via relays through other brainstem nuclei, including the **superior olivary nucleus** and a nucleus embedded within the lateral lemniscal fibers, called the **nucleus of the lateral lemniscus**. In all amniotes, the auditory part of the roof of the midbrain projects, via the dorsal thalamus, to the telencephalon.

In the ancestral stock of mammals, bony elements of the jaw were incorporated into the middle ear (see Fig. 9-1), which allowed for the conduction of higher frequency sounds to the oval window and the auditory receptive neural apparatus, the cochlea. This change is correlated with the presence of additional, phylogenetically new nuclei in the auditory brainstem of mammals. A number of the major nuclei present in mammals, however, are thought to be homologous to auditory nuclei in nonmammalian amniotes.

Of the cochlear nuclei present in mammals, the **anteroventral cochlear nucleus** appears to be homologous to the nucleus magnocellularis of nonmammalian amniotes, whereas the **posteroventral** and **dorsal cochlear nuclei** appear to be homologous as a field to nucleus angularis. The **medial superior olive** in mammals appears to be homologous to nucleus laminaris of nonmammalian amniotes, while the mammalian **lateral superior olive** is the homologue of the superior olivary nucleus of nonmammals. Ascending pathways, directly and indirectly to the midbrain roof, and thence via the dorsal thalamus to the telencephalon, similar to the ascending auditory pathways in nonmammalian amniotes, are present in mammals.

The vestibular nerve is relatively conservative among tetrapods, terminating in vestibular nuclei that lie in the same region of the medulla as the auditory nuclei. Two vestibular nuclei, a **superior** and a **lateral**, have been reported in anurans, with a possibility of two additional nuclei. In reptiles, four nuclei have been described: **dorsolateral**, **ventrolateral**,

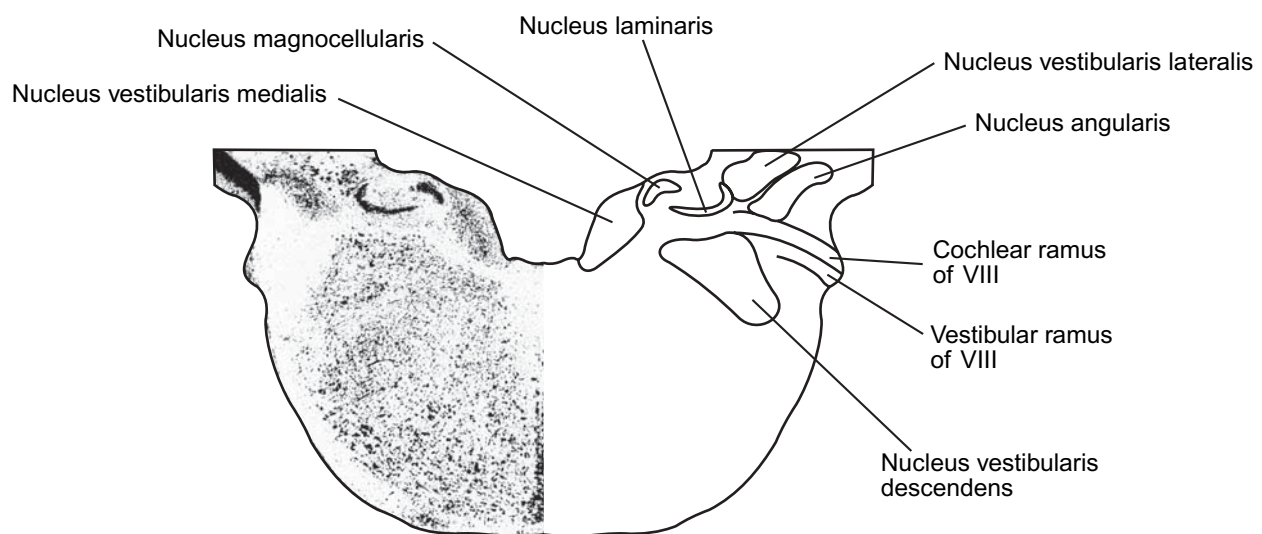


FIGURE 11-13. Drawing of a transverse section through the hindbrain of a bird (*Columba livia*) showing the positions of the octaval nuclei. Adapted from Karten and Hodos (1967) and used with permission of The Johns Hopkins University Press.

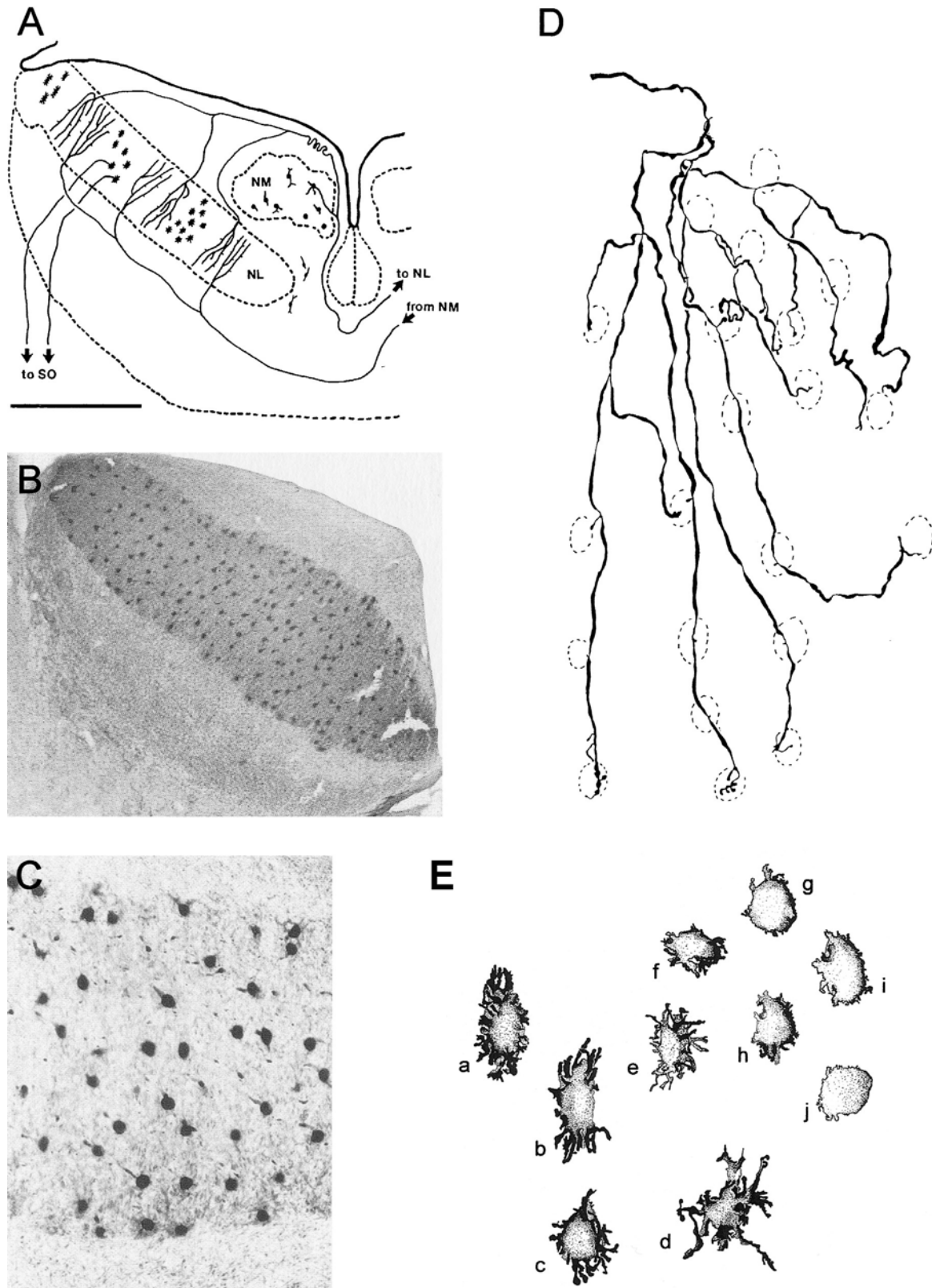


FIGURE 11-14. The auditory hindbrain nuclei in the barn owl (*Tyto alba*). (A) Drawing of a transverse hemisection through the medulla. The midline is at the right. Abbreviations: NL, nucleus laminaris; NM, nucleus magnocellularis; SO, superior olivary nucleus. (B) Photomicrograph of nucleus laminaris, oriented the same way as shown in A. (C) Enlargement of the individual neurons within nucleus laminaris. (D) Drawing of afferent auditory neuronal processes ending on individual neurons within nucleus laminaris. (E) Drawings of nucleus laminaris neurons. All elements of this figure were adapted from Carr and Boudreau (1993) and used with permission of John Wiley & Sons.

ventromedial, and **descending**. The most complex organization of the vestibular nuclei has been found in birds, which have six nuclei: **descending**, **medial**, **rostral**, **tangential**, **dorsolateral**, and **lateral**. In the mallard duck, projections have been identified that originate in the vestibular nuclei and innervate the motor nuclei for the craniocervical musculature, the complex set of muscles in the long neck. Some of these projections are direct ones and are probably involved in the vestibulocollic reflex for neck movements in response to vestibular stimulation, while others are via the reticular formation and thus involved in the more complex movements for head positioning during feeding and preening (see Chapter 13). In mammals, **superior**, **lateral**, **medial**, and **inferior vestibular nuclei** have been identified. The vestibular nuclei project to the cerebellum, some of the other motor cranial nerve nuclei, and the spinal cord. The vestibulospinal projections innervate motor neurons that innervate extensor muscles of the limbs and trunk. The vestibular nuclei also give rise to ascending projections to a region related to the somatosensory part of the dorsal thalamus.

A unique specialization of the vestibular system occurs in birds. A small sense organ, the paratympanic organ, is present in the avian middle ear. It contains mechanoreceptive hair cells, which may be involved in baroreception. Elastic ligaments in the middle ear may stretch in response to barometric pressure and stimulate the paratympanic organ. The organ is innervated by branches of the facial nerve (VII), but the nerve fibers project to vestibular and cerebellar nuclei. The latter projections of the paratympanic organ are similar to those of the spiracular organ of cartilaginous fishes discussed above. Both of these organs develop embryologically in association with the hyomandibular cleft. Corresponding organs are absent in lampreys, teleosts, amphibians, reptiles, and most or all mammals, but their similar developmental and innervation patterns in cartilaginous fishes and birds may be due to a shared generative basis.

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12

Motor Cranial Nerves

INTRODUCTION

Like the sensory cranial nerves, the motor cranial nerves fall into three distinct categories: dorsal cranial nerves, ventral cranial nerves, and parasympathetic components that innervate organs such as the salivary glands. The head provides a site of attachment for many muscles, both external and internal. The dorsal cranial nerves innervate the external (more lateral) muscles of the head, which constitute the branchiomeric muscles, whereas the ventral cranial nerves innervate the internal (more medial) muscles. For reference, Table 12-1 lists the motor cranial nerve components and gives their traditional and new classifications, the nucleus that gives rise to the component (and the parasympathetic ganglion or ganglia where appropriate), the effector organ, and the main functions for each component. This table is based predominantly on the human, as representative of the mammalian condition. Table 12-1 shows this new classification as it applies specifically to the motor components of the cranial nerves.

Muscles that can be categorized as internal muscles of the head include those within the orbits and those that form the tongue. Their innervation is summarized in Figure 12-1. Muscles within the orbits (eye sockets) move the eyes and are innervated by a set of three ventral cranial nerves, called the oculomotor nerves. The other internal muscles that form the tongue are innervated by the most caudal of the four ventral cranial nerves, the hypoglossal nerve. One of the most important roles of the tongue in terrestrial vertebrates is its use in feeding and swallowing, which we will consider in detail here. Over the course of evolution among tetrapods, additional uses

of the tongue for a variety of other purposes were also selected for, including as a tasting organ for substances that it manipulates (all tetrapods), a sticky instrument for the capture of prey (frogs, salamanders, and anteaters), an instrument for grooming the animal itself or grooming others (many mammals), a device for conducting pheromones (chemical signals) into the vomeronasal organ (many reptiles and mammals), and a tool for boring into trees in search of insect prey (woodpeckers). Another role for the tongue, one that is very likely derived from its ability to modulate the flow of a column of water on its way into the throat, is its ability to modulate the flow of a column of air on its way out of the throat. When such an air column is used for vocal communication as in vocalizing mammals, birds, and reptiles, the tongue also becomes an important part of this communication system.

The branchiomeric muscles of the head lie on the external surface of the skull and operate the jaws, the eyelids, the nostrils, the external ears, the scalp, the lips, the cheeks, and the eyebrows in those animals that possess such organs. Other branchiomeric muscles are attached at one end to the head and at the other end to the body skeleton and move the head itself in those animals with a moveable head. Finally, two branchiomeric muscles that are external in most vertebrates are located within the middle ear in mammals and are involved in protecting the delicate inner ear mechanisms from intense sounds. The majority of the external muscles of the head are controlled by motor neurons whose axons exit the brainstem by way of the trigeminal and dorsal facial nerves (Fig. 12-2). In this chapter, we will first address the control of feeding and swallowing and the cranial nerves involved in these processes, as well as the correlated parasympathetic innervation of glands in the head and of

TABLE 12-1. Classification, Nucleus and Ganglion, Effector Organ, and Functions of the Motor Cranial Nerve Components

Nerve or Nerve Component	New Classification (Traditional ^a Classification)	Nucleus & ganglion (or ganglia)	Effector Organ	Function
III Oculomotor	Somatic Efferent (GSE)	Oculomotor nucleus	Most extraocular muscles and levator palpebrae	Movements of the eyeball
	Visceral Efferent (GVE)	Edinger-Westphal nucleus of the oculomotor complex & ciliary ganglion	Ciliary and sphincter pupillae muscles	Accommodation and pupillary constriction
IV Trochlear	Somatic Efferent (GSE)	Trochlear nucleus	Superior oblique muscle	Movements of the eyeball
V Trigeminal	Somatic Efferent-Branchiomeric (SVE)	Trigeminal motor nucleus	Muscles of the jaw and tensor tympani	Chewing and damping loud sounds
VI Abducens	Somatic Efferent (GSE)	Abducens nucleus	Lateral rectus muscle	Movements (abduction) of the eyeball
VII _D Dorsal Facial	Somatic Efferent-Branchiomeric (SVE)	Facial motor nucleus	Muscles of facial expression and stapedius muscle	Movements of facial muscles and damping loud sounds
	Visceral Efferent (GVE)	Superior salivatory nucleus & pterygopalatine and submandibular ganglia	Lacrimal gland and sublingual and submandibular salivary glands	Production of tears and saliva
IX _D Dorsal Glossopharyngeal	Somatic Efferent-Branchiomeric (SVE)	Nucleus ambiguus	Stylopharyngeus muscle	Movement of the pharynx (throat)
	Visceral Efferent (GVE)	Inferior salivatory nucleus & otic ganglion	Parotid salivary gland	Production of saliva
X _D Dorsal Vagus	Somatic Efferent-Branchiomeric (SVE)	Nucleus ambiguus	Palate, pharynx, and larynx muscles	Movements of the throat and vocal cords
	Visceral Efferent (GVE)	Dorsal motor nucleus of the vagus & ganglia local to organs	Thoracic and abdominal viscera	Visceral movements and secretions
XI Spinal Accessory	Somatic Efferent-Branchiomeric (SVE)	Spinal accessory nucleus	Sternocleidomastoid muscle and the upper part of the trapezius muscle; larynx	Movements of the neck and shoulder; movements of the vocal cords
XII Hypoglossal	Somatic Efferent (GSE)	Hypoglossal nucleus	Muscles of the tongue	Movements of the tongue

^a GVE, General Visceral Efferent; GSE, General Somatic Efferent; SVE, Special Visceral Efferent

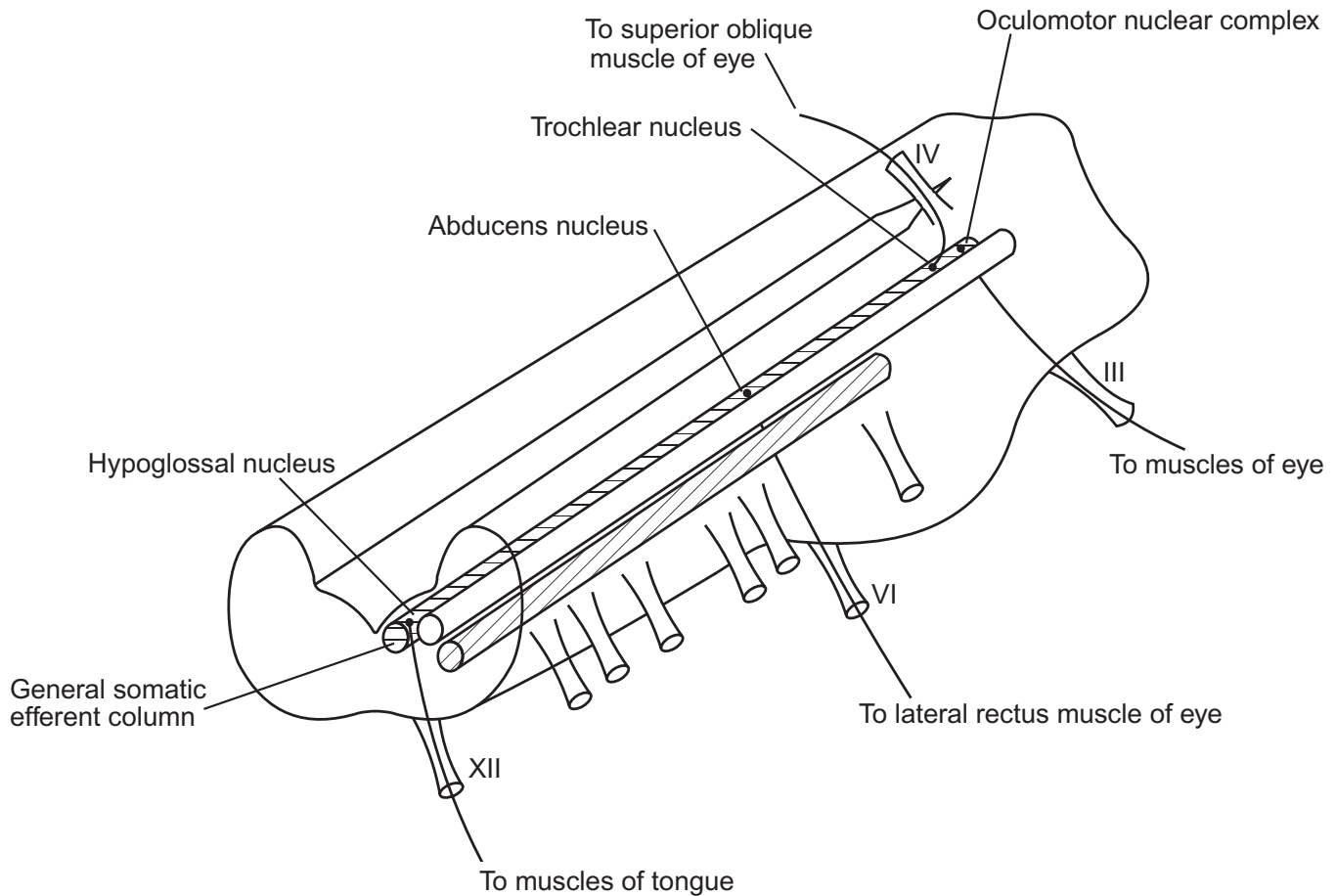


FIGURE 12-1. Schematic drawing of the ventral cranial nerve nuclei (III, IV, VI, and XII). Beginning at the rostral end of the brainstem (upper right), the nuclei of the oculomotor (III), trochlear (IV) and abducens (VI) nerves send axons to the extraocular muscles of the eyes. The hypoglossal nucleus (XII) controls the muscles of the tongue. These and other drawings in Chapter 12 are predominantly based on the human as representative of the generalized amniote condition.

the viscera (Fig. 12-3). We will then discuss another important function of the trigeminal and dorsal facial nerves, the acoustic reflex. Finally, we will consider the oculomotor muscles and their innervation (Fig. 12-1), as well as the correlated autonomic innervation of the lacrimal glands and internal eye structures (Fig. 12-3). An overview of all of the effector innervation discussed in this chapter is given in Figure 12-4.

The traditional classification of cranial nerves considers those nerves that innervate the internal muscles of the head as “general” and those that innervate the external, branchiomeric muscles as “special,” as discussed in Chapters 9 and 10. One of the major reasons for distinguishing two categories is the medial versus ventrolaterally migrated respective positions of the two sets of nuclei within the brainstem. In the spinal cord, however, the somatotopic arrangement of motor neurons in the ventral horn aligns with the muscles of the body such that medial neurons innervate proximal (i.e., more medial) muscles and lateral neurons distal (i.e., more lateral) muscles (see Chapter 8). Thus, the migrated position of the so-called “special” motor nuclei in the brainstem may simply be a somatotopic function of the more lateral, (i.e., external) position of

the branchiomeric head muscles versus the more medial ones. A further impediment to making a major distinction between the two groups of muscles and the nerves that innervate them is provided by the position of the abducens motor nucleus in at least some fishes. As will be discussed in Box 12-1 below, this nucleus, which is part of the traditionally classified general somatic motor column migrates to a ventrolateral position in goldfish, thus calling into question any distinction based on position. Table 12-1 indicates the new classification of the motor cranial nerve nuclei based on our current understanding of their embryological origins. For convenience in making the transition from the old classification, the old designations are given in parentheses.

FEEDING AND SWALLOWING

Animals that evolved in the water and have remained there throughout their history move food from the mouth into the throat and digestive tract by means of suction pressure. Animals that feed in air have to overcome the added difficulties of the

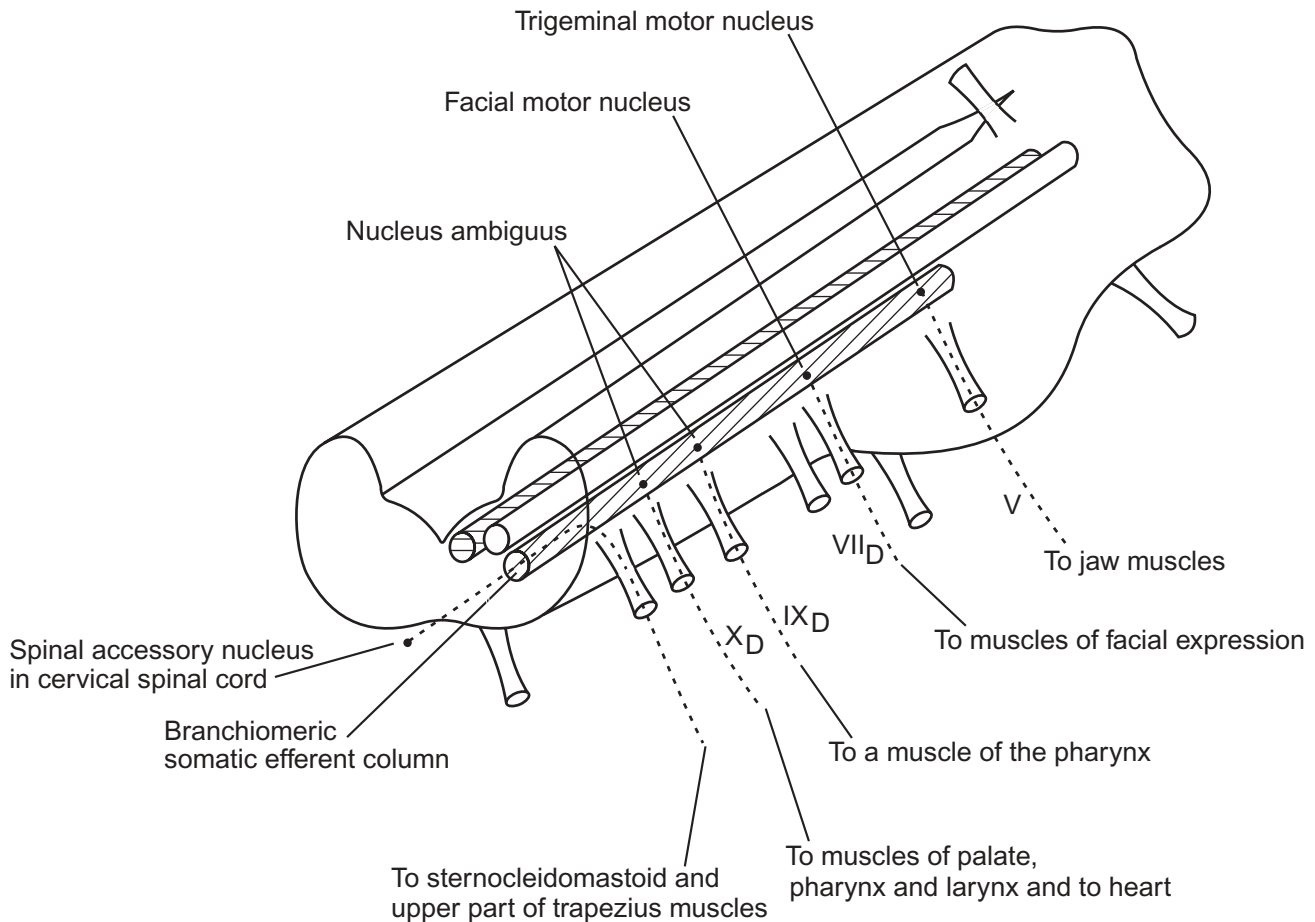


FIGURE 12-2. Schematic drawing illustrating the branchiomeric somatic efferent nuclei and nerves in the brainstem that innervate the muscles of the jaw, face, and throat. The motor nucleus of the trigeminal (V) nerve supplies axons to the muscles of the jaws and the tensor tympani muscle of the middle ear. The dorsal facial (VII_D) motor nucleus controls the muscles of the face, snout, external ear, and the stapedius muscle in the middle ear. Nucleus ambiguus sends axons to the muscles of the pharynx and throat via the dorsal glossopharyngeal (IX_D) and dorsal vagus (X_D) nerves. The spinal accessory nucleus (XI) innervates muscles of the neck and shoulder. Along with the dorsal vagus nerve, the cranial portion of the accessory nerve additionally innervates the larynx.

friction of the food with the sides of the mouth, the food's lack of buoyancy, and the pull of gravity. In the transition from life in the water to life on land, the bones of the head, especially those of the jaws, underwent considerable adaptive modification in response to the new selective pressures. Along with these changes came alterations in the muscles of the head that open and close the jaws. The early amphibian tetrapods had to deal with these selective pressures in order to feed in the terrestrial environment. Those that could manipulate the muscles of the hyoid arch (a bony remnant of the second visceral arch, located in the floor of the mouth) to help move food along in the mouth and throat were able to feed successfully in air. Eventually, other muscles derived from somites in the fifth (second metaotic) head segment became well developed and evolved into a specialized organ: the tongue.

The problems of feeding and swallowing are very different in water and in air. For example, filter feeding, in which

minute particles are sieved from the water being taken into the mouth, is only possible in an aquatic environment. Many aquatic feeders have evolved a negative-pressure mechanism that draws prey into the mouth. A number of terrestrial species have in fact readapted to aquatic feeding, such as turtles, crocodiles, penguins, and the various aquatic mammals (whales, porpoises, seals, otters, etc.), and some have reevolved suction feeding. In contrast, suction plays little role in the movement of food into and through the mouth and throat of air-feeding animals, except for drinking. Air-feeding animals instead depend on the tongue to move food through the mouth and into the throat for swallowing. In mammals, many of which chew their food to break it into smaller particles before swallowing, the tongue plays an important role in manipulating the food particles to and from the moving rows of teeth en route to the throat.

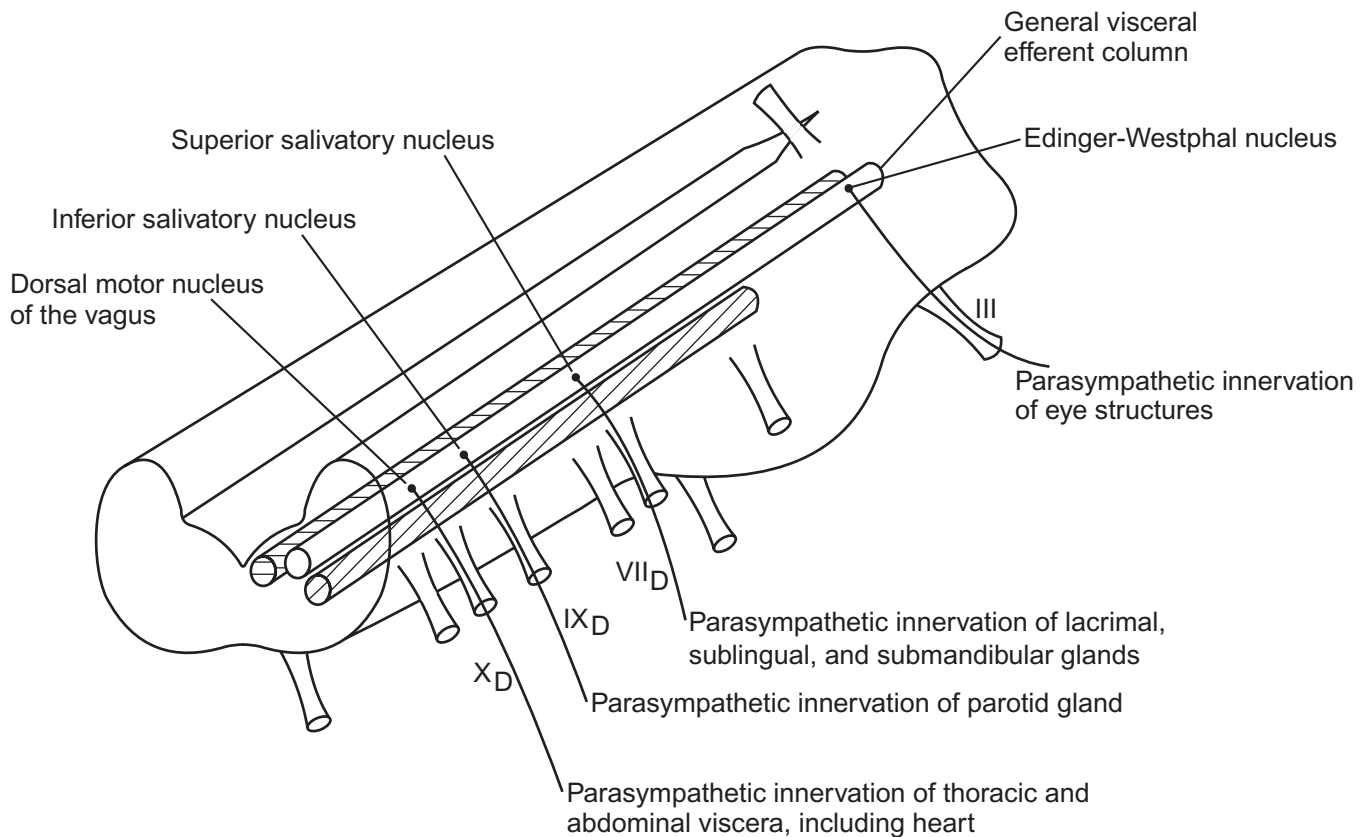


FIGURE 12-3. Schematic drawing illustrating the nuclei and preganglionic nerves in the brainstem for the parasympathetic nervous system. The Edinger-Westphal division of the oculomotor nuclear complex (III) supplies parasympathetic innervation to the ciliary muscle and the constrictor pupillae muscle. The superior salivatory nucleus (VII_D) supplies parasympathetic innervation for the lacrimal gland and two salivary glands (sublingual and submandibular), and the inferior salivatory nucleus (IX_D) supplies parasympathetic innervation to the parotid salivary gland. The dorsal motor nucleus of the vagus (X_D), along with a contribution from nucleus ambiguus for the heart, supplies parasympathetic innervation to the visceral organs of the thorax and abdomen.

The Neural Control of Feeding and Swallowing

The fleshy tongue, which is present only in tetrapods, is controlled by a group of neurons located at the caudal end of the medulla, near its junction with the spinal cord. The axons of these neurons form one of the ventral cranial nerves, the **hypoglossal nerve (XII)**, and their cell bodies are collectively called the **hypoglossal nucleus** (Fig. 12-1). The muscles of the tongue are complex, and their action is to change the shape of the tongue, as well as to raise and lower it and move it forward. Each muscle is controlled by a different group of neurons within the hypoglossal nucleus. The backward movement of the tongue is accomplished by muscles that elevate its hyoid skeleton. These muscles are innervated by axons of motor VII_D.

In birds, the terminology for the nucleus that innervates the tongue has been revised. The group of neurons previously called the hypoglossal nucleus actually innervates the musculature of the upper neck, so its name has been changed to the **supraspinal nucleus**. The cell group previously called nucleus intermedius, which lies ventral to the dorsal motor nucleus of

X in the region of the obex, innervates the tongue and is now correctly called the **hypoglossal nucleus**.

Neurons that form the nucleus of VII_D, the **motor nucleus of the dorsal facial nerve**, lie in the branchiomeric somatic efferent column of the brainstem (Fig. 12-1), rostral to the hypoglossal nucleus. In addition to innervating muscles of the hyoid apparatus, the efferent axons of **motor VII_D** innervate the superficial muscles of the head, including muscles of the cheeks, lips, nares (nostrils), and the forehead muscles. In mammals, in which the muscles of the head and face are very well developed, motor VII_D controls the movements of the pinna of the ear, which is the external, sound-collecting portion of the ear, as well as the muscles of facial expression (lips, cheeks, eyebrows, etc.), which in some species are very important in social communications such as those of aggression and appeasement. It also contributes, along with the oculomotor nerve and sympathetic fibers, to the innervation of the muscles of the eyelid. The **motor nucleus of the trigeminal nerve** (motor V) (see Fig. 16-8) lies in the branchiomeric somatic efferent column rostral to motor VII_D. The efferents of **motor V** exit the brainstem through the mandibular branch of V and terminate on the muscles of the jaws.

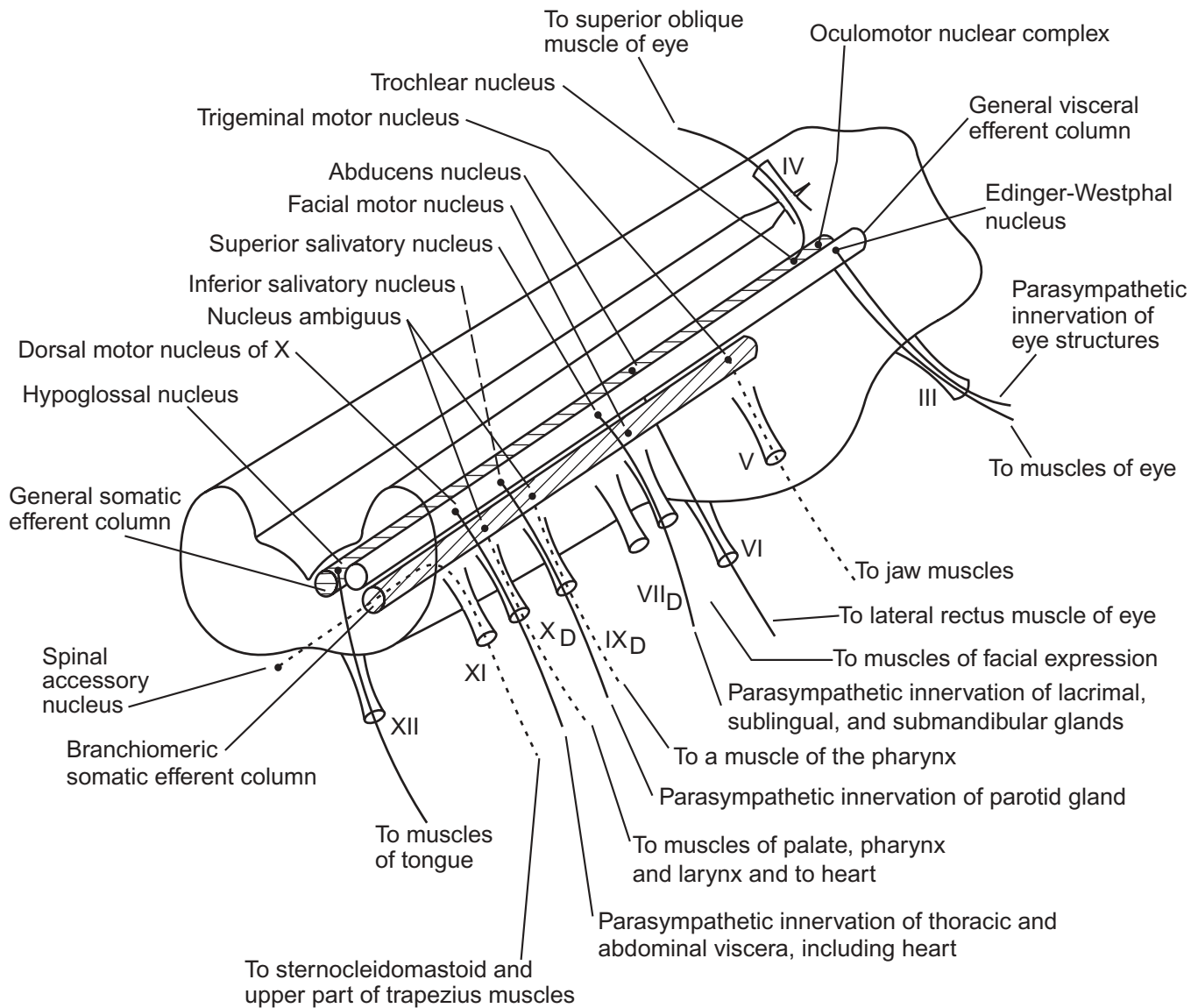


FIGURE 12-4. Schematic drawing illustrating all of the motor and preganglionic nuclei in the brainstem that innervate the muscles and glands of the head in a mammal. This figure includes all of the components shown in Figures 12-1, 12-2, and 12-3 to serve as an overall reference.

Two important influences over the actions of motor V and motor VII_D are the senses of taste and touch. The gustatory nucleus and the descending nucleus of V are the central cell populations that receive the incoming taste and somatic axons, as discussed in Chapter 11. These cell groups, in turn, send some of their axons directly to motor neurons of the somatic efferent column that control muscles of the head, as well as to cell populations of the reticular formation. These reticular formation cell groups, scattered throughout the brainstem, serve to coordinate various reflexes and voluntary motor behavior. They also serve to integrate information from various senses. For example, a fish might detect something edible in the nearby water; not only would the reticular formation coordinate the activities of motor V and motor VII_D, so that the muscles of the jaws and face would produce the necessary suction to ingest the food, but it would also stimulate or inhibit the activities of the oculomotor nerves in order to move the eyes in the

direction of the food source so that both visual and gustatory information could be coordinated.

In air-feeding animals, motor V and motor VII_D control muscles of the jaws that press the food objects against the roof of the mouth and manipulate them in the direction of the throat. Of crucial importance to these motor responses are inputs from the mesencephalic nucleus of V, which provides feedback from the muscles of the jaws (see Fig. 11-2). Ascending sensory pathways to the telencephalon via the dorsal thalamus and descending motor pathways from the telencephalon to the reticular formation also play a role in the integration and coordination of these very precise and complex movements.

In ray-finned fishes, such as catfishes and carps, which have excellent gustatory systems, motor V receives projections from the facial lobe (see Chapter 11). Motor V and motor VII_D also receive projections from the descending nucleus of V, the cerebellum, and the midbrain tectum. These connections may

serve to coordinate opening and closing of the mouth in relation to other sensory systems such as somatosensory, vestibular, and lateral line. Motor V also receives axons from the reticular formation and the hypothalamus. In addition, reciprocal connections between motor V and motor VII_D serve to further coordinate their activities. Although motor V and motor VII_D control the ingestion of food into the mouth, swallowing is under the control of neurons located farther caudally, in a nucleus called **nucleus ambiguus**. This nucleus sends its efferent axons via the dorsal glossopharyngeal (IX_D), dorsal vagus (X_D), and accessory (XI) nerves to the muscles of the pharynx, larynx, and palate. Nucleus ambiguus receives projections from the vagal (X_{VI}) lobe, which, together with the facial (VII_{VI}) lobe, is an expansion of the gustatory region of the caudal medulla. Thus, the facial gustatory system appears to be an ingestive system, whereas the vagal gustatory system appears to be a swallowing system.

Motor V is well developed in birds, of which pigeons and ducks have been the most extensively studied. These studies have described the mechanisms for operation of the jaws during various motor acts related to feeding, such as opening the mouth in proportion to the size of the object to be taken in, pecking, grasping, manipulation of food in the mouth and throat, and swallowing. Motor V is also well developed in those mammals that chew their food.

In air-feeding animals, the lack of a water column to lubricate the food has been compensated for by the evolution of the salivary glands. These glands are present only in amniotes and are controlled by the parasympathetic nervous system. Their postganglionic fibers are innervated by axons from the parasympathetic components of motor VII_D and motor IX_D (Fig. 12-1). Salivary glands provide not only lubrication of food; they are also essential for the grooming behaviors in a number of groups of mammals, which involve the jaws and teeth as well as the tongue. In some snakes, the salivary glands produce neurotoxins and/or anticoagulants. The neurons of the parasympathetic division of motor VII_D form the **superior salivatory nucleus**; this nucleus controls the submandibular and sublingual salivary glands in the lower jaw. The parasympathetic division of motor IX_D consists of the neurons in the **inferior salivatory nucleus**, which innervates the parotid and infra-orbital salivary glands in the upper jaw. The latter gland is absent in humans.

The Communication Systems of Fishes

Some fully aquatic animals have developed communication systems that equal and sometimes surpass the communication systems of land animals that live in air. These aquatic systems include some that produce sounds as well as others that utilize a system of electrical communication. These systems involve some of the same cranial nerves as those used for feeding and swallowing plus efferent nerves from additional hindbrain motor cell groups and, in some cases, some spinal nerves as well. Because the efferent nerves of the additional hindbrain motor cell groups for these systems, such as the sonic motor nucleus, are so uniquely evolved, they are not traditionally classified as cranial or spinal nerves per se. Perhaps some future classification will include them. These aquatic communication systems have some striking similarities, most likely as the result of convergent evolution, to the auditory and

vocal systems of tetrapods, as may be seen by a comparison with figures in Chapter 28.

Sonic Motor System. Some fishes are capable of generating vocalizations without an air column by rhythmically contracting and relaxing special muscles called **sonic muscles** attached to the taut swim bladder. The effect is something like beating on a drum. These vocalizations function in courtship and territorial behavior. The sonic muscle is innervated by neurons in the **sonic motor nucleus**, which is located in the caudal medulla. This nucleus shows sexual dimorphism; i.e., it is larger in males. The nucleus may be generatively homologous (see Chapter 1) to part of the hypoglossal nucleus of tetrapods. The sonic motor system as a whole bears a striking resemblance to many features of the vocal control systems of tetrapods (see Chapter 28 and Box 28-1).

Figure 12-5 shows the sonic motor system of the plainfin midshipman (*Porichthys notatus*), one of several species of

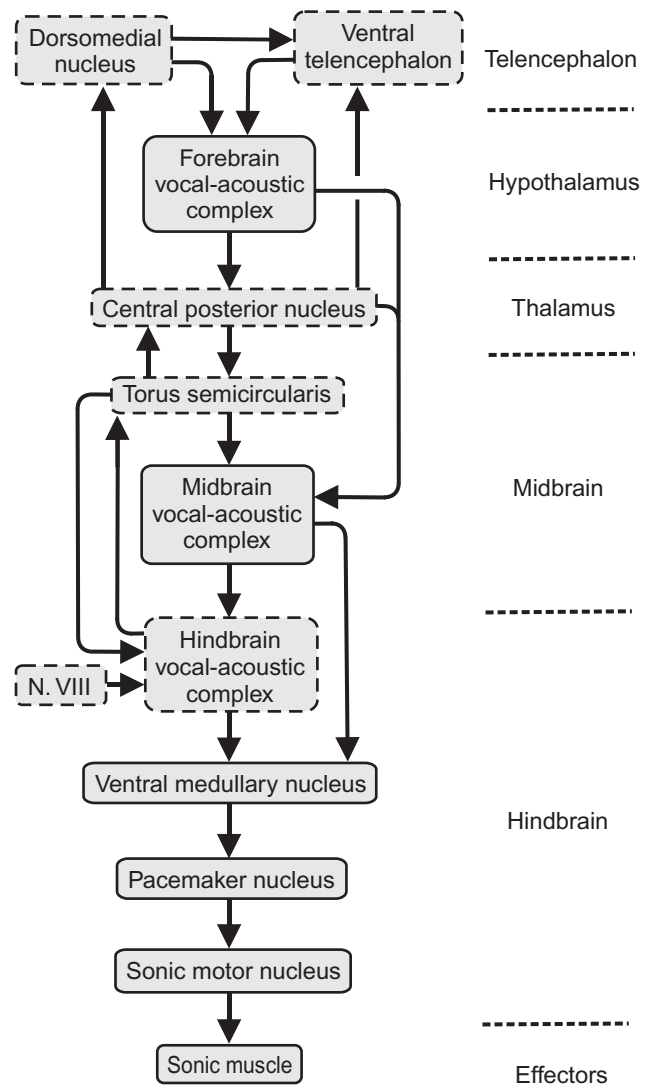


FIGURE 12-5. The vocal-acoustic pathway of the plainfin midshipman (*Porichthys notatus*). Nuclei or groups of nuclei that are auditory or have major connections with the auditory system are shown with broken borders. Based on Goodson and Bass (2002).

vocalizing fishes. The diagram, based on the work of Andrew Bass and his colleagues, shows the strong interrelationships between the sonic motor system and the auditory system of this animal. The ascending auditory pathways [comparable to the general scheme shown in Fig. 3-16(A)] from the hindbrain vocal-acoustic complex (including the cochlear nuclei) to the torus semicircularis in the midbrain, thence to the central posterior nucleus of the thalamus, and finally to part of the telencephalon (the dorsomedial nucleus), are shown on the left side of the diagram. The telencephalon is the source of a complex sequence of descending relays to the hindbrain nuclei that control the production of vocalizations. Like the respiratory vocal system of tetrapods, the midshipman's sonic motor nucleus is driven by a premotor or **pacemaker nucleus**, which is in turn controlled by the **ventral medullary nucleus**. In addition, three aggregations of nuclei are shown at different levels of the neuraxis as **vocal-acoustic complexes**: one in the hindbrain, one in the midbrain, and one in the telencephalon. Each complex consists of several nuclear groups that function together in the sonic-auditory process. Thus, the **hindbrain vocal-acoustic complex** contains the main auditory nuclei of the hindbrain: the **descending and secondary octaval nuclei** as well as a column of **paraventricular neurons** near the vestibular nuclei. The **midbrain vocal-acoustic complex** contains the **periaqueductal grey**, which plays an important role in tetrapod vocalization (see Chapter 28), and the **paralemniscal tegmentum**. The **forebrain vocal-acoustic complex**, which is located in the hypothalamus, contains the **anterior tuberal nucleus**, the **ventral tuberal region**, and the **parvocellular preoptic area**.

Gymnotid Electrocommunication System. Although the subjects of this section are the auditory-related and vocal-respiratory systems, which are crucial for communication in many animal species, it does seem fitting to include mention here of a nonauditory, nonvocal sensory-communication system, the electrosensory-electromotor system, because it seems to follow a number of the same organizational principles as the auditory-vocal system. The electrosensory pathway is a collothalamoc pathway that is organized along similar lines to those of the auditory system (see Figure 3-16). Figure 12-6 shows the electromotor pathway in a gymnotid fish, which has a similar organization to the vocal-respiratory pathways of tetrapods and the sonic motor pathway of vocalizing fishes. From the **electrosensory torus semicircularis** in the midbrain, the ascending pathway continues to the diencephalic **nucleus electrosensorius**, which is found in gymnotids but not in mormyrids. The efferents of the nucleus electrosensorius terminate in the diencephalic **prepacemaker nucleus complex**, which consists of a **dorsomedial division** and a **ventrolateral division**. This complex also has two-way connections with the **ventral nucleus of the ventral telencephalon**. Both divisions of the prepacemaker complex project to the **pacemaker nucleus** in the hindbrain. The pacemaker nucleus consists of two types of cells: the **pacemaker cells** and the **relay cells**. The efferents of the pacemaker cells are to the relay cells. The dorsomedial division of the prepacemaker complex projects to the pacemaker cells and to the ventrolateral division. The ventrolateral division projects directly to the relay cells. The efferents of the relay cells are to the **electromotor neurons** of the spinal cord that result in the elec-

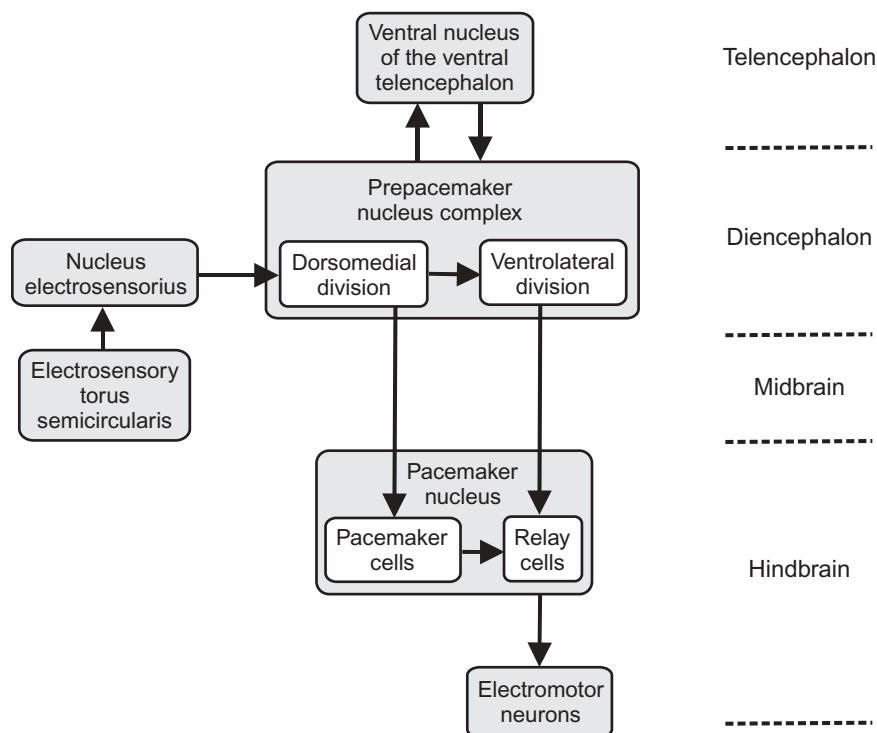


FIGURE 12-6. The electromotor command pathway of a gymnotid fish. Based on Metzner (1999).

tric organ discharge. In addition to electrosensory inputs to this system, there are also mechanosensory and olfactory inputs. For a more detailed description of this system, see a review by Metzner (1999).

In addition to its function in electrolocation of objects in the environment, electric organ discharges also play important roles in communication, among which are signals that allow for individual recognition. During encounters between individuals, gymnotids can modulate the discharge frequencies of their electric organs. When such signals are monitored by acoustic amplifiers and loudspeakers, they produce sounds that human observers characterize as “chirps.” Moreover, when two fish with similar discharge frequencies come within range of each other, they alter the frequency of their electric organ discharges so as to avoid interfering with each other’s signals. This is known as the **jamming avoidance response (JAR)**. Thus, a fish with the slightly lower frequency than that of the conspecific that it meets would lower its frequency further and a fish with a slightly higher frequency would increase its frequency.

Mormyrid Electrocommunication System. Figure 12-7 depicts the comparable electromotor pathway in mormyrid fishes. The pathway begins at the midbrain **pre-command nucleus** and continues to the **command nucleus** and the **medullary electromotor relay nucleus** of the hindbrain, next to the **spinal cord electromotor relay nucleus** and finally to the animal’s **electric organ**. Several interesting features of this sensory-motor system may be seen. First, the highest level of the electrosensory-electromotor pathway appears to be the midbrain. At present, forebrain components of this pathway have not been identified. Second, a corollary pathway from the command pathway to the electrosensory

lateral line lobe is present. This pathway informs the electrosensory lateral line lobe of the commands of the command generator neurons in the command nucleus. Similar corollary pathways have been reported in auditory-vocal pathways in fishes and tetrapods.

THE ACOUSTIC REFLEX

Among the more striking changes in the head in response to the transition from the aquatic to the terrestrial environment were those that involved the ear. Because air is a less dense medium for sound conduction than water, greater acoustic sensitivity was selected for in meeting the challenges of survival on land. Among the structural adaptations that resulted from this transition was the development of a chamber between the inner ear (in which the acoustic receptors are located) and the outer ear (which traps the sound waves from the surrounding environment). This chamber, the middle ear, is separated from the external ear by a membrane, the **tympanum** or ear drum. Initially, the middle ear contained a single bone, the **columella**, which was derived from the dorsal portion of the second visceral arch. The columella connected the tympanum to the inner ear and served to conduct sound to the entrance of the inner ear.

In the ancestral stock of mammals, two jaw bones, the **articular** and the **quadrate**, and the muscles that were attached to them, migrated toward the ear canal under the influence of selective pressures related to feeding (see Chapter 9). Once they were close to the ear canal, however, they invariably became involved in the conduction of sound, as are many of the bony structures in that region. At this point, their sound-conducting function became more important to the animal’s

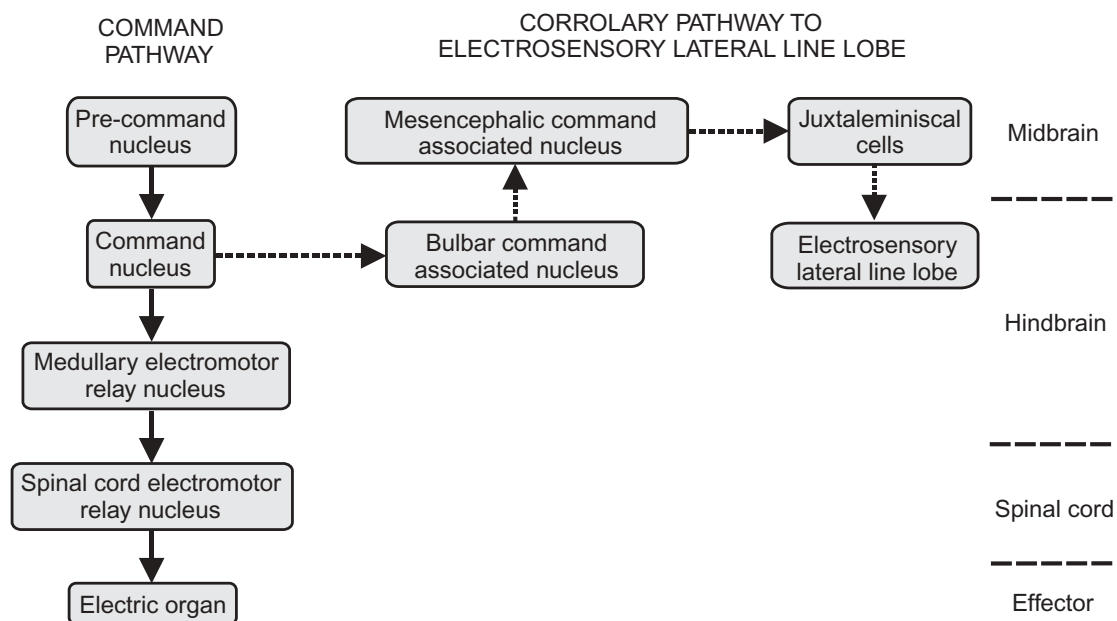


FIGURE 12-7. The electromotor command pathway of a mormyrid fish. The arrows with broken lines indicate the corollary pathway from the electromotor command pathway to the electrosensory lateral line lobe. Based on Meek and Grant (1994).

survival than did their feeding function, and selection favored the bones being more intimately involved in the hearing process. Eventually, they became incorporated into the middle ear and took their associated nerves and muscles along with them. Extant mammals thus possess three bones in their middle ears, which are collectively known as the **ossicles**. In the mammalian middle ear, the bone derived from the columella is called the **stapes**, and the bones derived from the articular and the quadrate are called the **malleus** and the **incus**, respectively.

Two muscles are attached to the ossicles: the **stapedius** and the **tensor tympani**. These muscles, together with the ossicles themselves, help to dampen intense sounds and thereby prevent damage to the acoustic receptors in the inner ear. This protective action is known as the **acoustic reflex**. Motor V innervates the tensor tympani, which inserts on the malleus, and motor VII_D innervates the stapedius, which inserts on the stapes. If you want to recall which nerve innervates which muscle, remember that “tensor tympani” and “trigeminal” all begin with the letter “t,” while “stapedius” and “seventh” begin with the letter “s.”

In mammals, sound waves from the external world pass down the ear canal and vibrate the tympanum (ear drum) at the entrance to the middle ear. The vibrations are transmitted via the ossicles in the middle ear to the oval window, which is the entrance to the cochlea. The cochlea, a bony structure shaped like a snail shell, from which its name is derived, contains the receptors for hearing (Chapter 2). The receptors activate axons of the cochlear ramus of the eighth nerve which terminate in the medulla in the dorsal and ventral cochlear nuclei. As discussed in Chapter 11, axons from these cochlear nuclei pass to a nearby cell group called the superior olivary nucleus. This is an important coordinating nucleus for auditory reflexes. The superior olivary nucleus sends its axons to motor V and motor VII_D, which control the tensor tympani and stapedius muscles in the middle ear. The tensor tympani increases tension on the tympanum, which decreases the intensity of sound entering the middle ear; the stapedius pulls the stapes away from the oval window, thereby reducing the intensity of the vibrations entering the cochlea.

MOTOR CONTROL OF EYE MUSCLES

For the overwhelming majority of vertebrates, the eyes are an important source of information about distant objects. For many animals, such as birds, the eyes are the most important source of information about the surrounding environment. The eyes receive assistance in their information-gathering task from the eye muscles. These muscles are of two types: **extraocular muscles**, located on the outside of the eye and innervated by three ventral cranial nerves, and **intraocular muscles**, located within the globe of the eye and innervated by parasympathetic fibers (see Fig. 12-2).

The Extraocular Muscles in Jawless Vertebrates

Hagfishes lack extraocular muscles altogether. Lampreys have extraocular muscles, but differences occur in the number and innervation pattern of the muscles compared with the

situation in jawed vertebrates. Fossil evidence from extinct osteostracan fishes (see Chapter 31) indicates that extraocular eye muscles were present as the plesiomorphic condition for vertebrates and that hagfishes have secondarily lost them.

In lampreys, two oblique extraocular muscles are present, a **rostral oblique muscle** innervated by cranial nerve III and a **caudal oblique muscle** innervated by cranial nerve IV, which appear to be homologous to the inferior and superior oblique muscles of jawed vertebrates, respectively. Three, rather than four, recti are present in the main group of extraocular muscles. The **dorsal** and **rostral rectus muscles** of lampreys are innervated by cranial nerve III and appear to be homologous to the superior and inferior recti of jawed vertebrates, respectively. The **ventral rectus muscle** of lampreys is innervated by cranial nerve VI and corresponds to the lateral rectus muscle of jawed vertebrates. A medial (or nasal) rectus muscle is absent in lampreys. Lampreys, like jawed vertebrates, have a muscle that retracts the globe of the eye and is innervated by an accessory abducens nucleus; in lampreys, this muscle is called the **caudal rectus muscle**.

The Extraocular Muscles in Jawed Vertebrates

Many animals have panoramic or near-panoramic vision, which means that they can see in all directions (or nearly so) without moving their eyes. These animals have their eyes situated on the sides of the head, as many birds have, or near the top of the head, as do amphibians and reptiles. Such animals still need to move their eyes in order to place objects into the zone of most acute vision on the retina. The extraocular muscles serve to move the eyes so that the center of gaze can be shifted from one position in space to another. The extraocular muscles also produce micromovements of the eyes so that images that fall on the retina do not remain constantly on the same receptors. Without these micromovements of the eye, the receptors would soon fatigue and the image would fade away. The major extraocular muscles comprise four rectus muscles—the **inferior rectus**, **superior rectus**, **medial rectus**, and **posterior** (or lateral) **rectus**—and two oblique muscles—the **inferior oblique** and **superior oblique**.

Four of the extraocular muscles are innervated by the **oculomotor nerve (III)**: the superior, inferior, and medial rectus muscles and the inferior oblique muscle. The **trochlear nerve (IV)** innervates only the superior oblique muscle, and the **abducens nerve (VI)** innervates only the lateral rectus muscle. The sensory innervation of the extraocular muscles (primarily for position sense) is via the ophthalmic division of the trigeminal nerve (V). Table 12-2 lists the extraocular muscles that are most commonly found in jawed vertebrates and their cranial nerve motor innervation. The presence of four recti and two oblique muscles is plesiomorphic for at least jawed vertebrates.

In addition to the muscles that move the eyes, another extraocular muscle controls the eyelid. In those animals that have movable eyelids (amphibians and amniotes), the upper lid is raised by the **levator palpebrae muscle** or the lower lid is dropped by the **depressor palpebrae muscle**. The levator palpebrae muscle is innervated by cranial nerve III but receives additional innervation from sympathetic fibers, and a third contribution to eyelid movement comes from cranial nerve VII,

TABLE 12-2. Innervation of Extraocular Muscles in Jawed Vertebrates

Muscle	Nerve	Function
Inferior oblique	III	Rotates eye upward and outward
Superior oblique	IV	Rotates eye downward and outward
Inferior rectus	III	Rotates eye downward and inward
Superior rectus	III	Rotates eye upward and inward
Medial rectus	III	Rotates eye medially
Posterior (lateral) rectus	VI	Rotates eye laterally
Levator palpebrae superioris	III	Raises upper eyelid
Depressor palpebrae inferioris ^a	V	Lowers lower eyelid
Retractor bulbi ^b	VI	Retracts globe of the eye; advances nictitating membrane
Pyramidalis ^c	III	Advances nictitating membrane
Quadratus ^d	III	Advances nictitating membrane

^a Amphibians, reptiles, and some mammals.
^b Birds, crocodilians, turtles, and most mammals.
^c Birds and lizards.
^d Amphibians, birds, and reptiles.

which innervates the orbicularis oculi muscle. This muscle encircles the eye and also sends slips into the eyelid.

Another function of the extraocular eye muscles is to control the **nictitating membrane** or so-called “third eyelid.” The nictitating membrane is an internal eyelid that provides an additional layer of protection to the cornea of the eye and aids in the distribution of the tear film. It is present in reptiles and birds and in some amphibians and mammals. Among mammals, the membrane is present in carnivores, rabbits, and hares but not in primates. Some bottom-feeding ray-finned fishes and sharks have a similar protective membrane.

The action of this internal eyelid is quite different from that of the external eyelids. The latter are actively operated by muscles that open and close the lids. The nictitating membrane, however, is passively operated. The membrane slides in front of the cornea when the eyeball is retracted farther into the eye-socket by a special extraocular muscle, the **retractor bulbi**. In some reptiles, the retractor bulbi is assisted by one of two additional muscles: the **quadratus** (lizards) or the **pyramidalis** (crocodiles and turtles). In birds, the globe of the eye fits so tightly into the eyesocket that little room is left for retraction. Therefore, the retractor bulbi is not present and in its place are both the quadratus and the pyramidalis muscles. These muscles

act to slide the nictitating membrane over the cornea without retraction of the eye.

Movement of the eyes is not the only use of the extraocular muscles. In an electric fish known as *Astroscopus* (the stargazer), these muscles have been independently modified to form electric organs, similar to the somatic electric organs of the electric eel and other electric fishes. The stargazer lies buried in the sand of the sea floor with only its eyes exposed. When prey approach closely, they are stunned by discharges from the electric organs. In spite of this dramatic change in function of the extraocular muscles, their innervation remains the oculomotor nerve.

In land animals, the lack of a water column to lubricate the surface of the eyes has been compensated for by the evolution of the lacrimal glands. These glands are present only in amniotes and are controlled by the parasympathetic nervous system. Their postganglionic fibers are innervated by axons from the parasympathetic component of motor VII_D (Fig. 12-1). The neurons of the parasympathetic division of motor VII_D form the **superior salivatory nucleus**; some of their postganglionic neurons innervate the lacrimal gland (Fig. 12-3).

The Intraocular Muscles

The intraocular eye muscles do not move the eye; rather, they control the action of structures within the eye. The iris is one such structure; it is opened and closed in response to the level of illumination of the retina by a pair of muscles: the **dilator pupillae**, which increases the diameter of the pupil, and the **sphincter pupillae**, which decreases the diameter. Another intraocular muscle, the **ciliary muscle**, controls the curvature of the lens to permit accommodation, which is the ability of the eye to focus on close objects.

The intraocular muscles, except the dilator pupillae, are innervated by parasympathetic fibers. Neuron cell bodies of the parasympathetic component of the oculomotor nerve lie within the **Edinger-Westphal nucleus** (Fig. 12-2) within the oculomotor complex. Their axons course to the **ciliary ganglion** via the oculomotor nerve. Postganglionic parasympathetic fibers from the ciliary ganglion innervate the intraocular muscles. In contrast, the dilator pupillae is innervated by fibers of the sympathetic nervous system.

Central Control of the Eye Muscles

The characteristic appearance and, in most vertebrate taxa, the consistent position of the nuclei of the cranial nerves that control the eye muscles make them easy to identify (Fig. 12-2). These nuclei are located just below the floor of the third ventricle. The oculomotor nucleus (III) and the trochlear nucleus (IV) usually are located rather close to one another. The abducens nucleus (VI) is separated from III and IV in the caudal direction. In animals with a retractor bulbi, an accessory abducens nucleus is present, which controls this muscle.

In lampreys, the trochlear and abducens nuclei lie in a position that conflicts with the generally accepted interpretation of the somatic motor column. Trochlear motor neurons have a ventrostral position early in development but then migrate to a dorsal position in the cerebellar plate, a position

BOX 12-1. The Unusual Abducens Nucleus of Goldfish: A General Somatic Efferent Nucleus “Gone Walkabout”

The oculomotor (III), trochlear (IV), and abducens (VI) motor nuclei lie in a dorsal and medial position within the brainstem tegmentum in most vertebrates. They are traditionally classified as general somatic efferent based substantially on their position, as noted above. A salient exception to the general rule is provided by the abducens nucleus in at least some bony fishes. Angel Pastor, Blas Torres, Cosme Salas, and their colleagues studied the functional organization of eye movement control in goldfish. They examined the influence of the optic tectum, cerebellum, octaval nuclei, and other structures on eye movements via their patterns of connectivity with the oculomotor, trochlear, and abducens motor nuclei, as well as the peripheral innervation patterns of these nuclei to the extraocular muscles.

The oculomotor and trochlear nuclei are located in the same dorsomedial position within the tegmentum as in other vertebrates. In contrast, the abducens nucleus consists of two divisions, rostral and caudal, which are both located close to the ventral surface of the brainstem (Fig. 1). In position, this nucleus thus mimics the behavior and position of nuclei of the traditionally recognized “special visceral” efferent column. The migration of cranial nerve motor neuronal cell groups in the brainstem may thus be more a function of simple somatotopic mapping, as considered above, than of any fundamental difference in their nature. The extraocular muscle that the abducens nerve innervates is the lateral rectus, which is the most lateral of the extraoc-

ular muscles. In this context, the migrated position of the abducens nucleus in goldfish may not be an inexplicable oddity after all. As discussed elsewhere in this chapter, both the trochlear and abducens nuclei are also migrated in lampreys.

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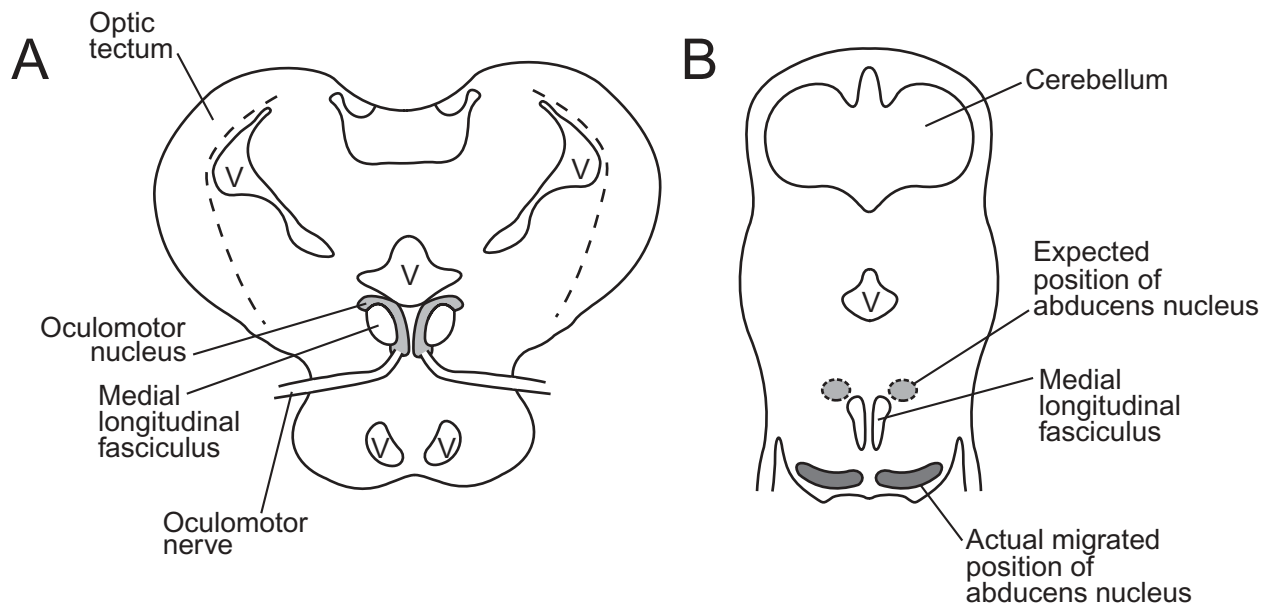


FIGURE 1. Drawings of transverse sections through the (A) midbrain and (B) hindbrain of a goldfish. The oculomotor nucleus is in its expected location in the midbrain (A), while the abducens nucleus is migrated to a ventral position in the hindbrain (B). The ventricular spaces are indicated by the abbreviation V. After Pastor et al. (1991).

BOX 12-2. The Ciliary Muscles of Diving Birds: A Magnificent Adaptation

The air and aqueous environments result in different optical constraints on the structures of the eye that focus the light rays onto the receptor layer of the retina. In fishes, the light rays pass through the cornea of the eye without significant bending. Because the water-cornea interface effectively neutralizes the optical power of the cornea, the light rays pass through the cornea without bending and then enter the spherical lens, which focuses them onto the retina. For land animals, however, the air-cornea interface results in the cornea becoming a powerful refractive element with considerable focusing power. Thus, the light rays pass from the air through the cornea and then into the aqueous environment of the external chamber of the eye with significant bending. The more oval-shaped lens of the typical land animal then provides additional focusing of the light rays onto the retina. In most land animals, the lens is not sufficiently spherical to be able to focus light rays when the land animal's head is placed under water; in other words, a land animal underwater is effectively far-sighted. The ciliary muscle, which develops from local, neural crest-derived mesenchyme, can adjust the curvature of the lens somewhat, but it is relatively small and unable to make up for the loss of corneal focusing in an external aqueous environment. This is the reason that humans need goggles in order to see well under water when snorkeling or diving. The goggles provide an air interface with the water, which allows the normal focusing contributions from both the cornea and the lens to operate.

Birds that dive go from air into water without the benefit of goggles. Some of the birds that live in the shore environment and obtain part or all of their food from the aquatic milieu do not need excellent vision when under the water. For example, the herring gull, *Larus argentatus*, is a scavenger and mostly feeds in the air environment. The pelican, *Pelecanus occidentalis*, dives into the water almost perpendicularly and catches fish that happen to be in the path of its large, open beak. The mallard duck, *Anas platyrhynchos*, is herbivorous and feeds on underwater vegetation. Such birds as these do not have specialized optical adaptations.

Other shore birds—including the cormorant *Phalacrocorax auritus*, the merganser duck *Mergus cucullatus*, and

the guillemot *Cepphus grille*—that dive to catch fish, crabs, and other aquatic life under the surface of the water have the exceptional challenge of needing to see with good focus in both the air and the aqueous environments. Jacob Sivak and his co-workers have studied the specialized anatomy of the intraocular muscles in these birds. Selective pressures over evolution have resulted in the dramatic changes to the ciliary and/or iris muscles such that they are large, powerful, striated muscles in these birds. When the bird dives, the ciliary muscle contracts forcefully and rapidly, drastically changing the shape of the lens so that the bird has almost instantaneous focus under water. Various specializations of the iris and the sclera in some species also assist in the process. When the bird has successfully captured its prey and returns to the surface of the water, the lens resumes its resting state, and the light rays can be focused by both the cornea and the lens as in the normal land animal condition. This adaptation thus allows these birds to occupy a rather selective niche utilizing the quick and accurate capture of fast-moving underwater prey for a food source. Similar adaptations to the eye have also been found in the penguin, *Spheniscus magellanicus*. A question that needs to be asked is whether diving birds have a particularly large Edinger-Westphal nucleus, as one might expect them to for innervation of their large ciliary muscle.

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that is topologically a rostral continuum of the trigeminal motor nucleus and implies that these neurons are branchial rather than somatic. Abducens motor neurons also migrate, and their axons exit the brainstem with the trigeminal root.

The Oculomotor Complex

The oculomotor nucleus (III) is often considered along with several related nuclei as part of an **oculomotor complex**. In fishes such as the stargazer, in which the extraoc-

ular muscles have become specialized as electric organs, the oculomotor nucleus consists of an **oculomotor division** and an **electromotor division**. The oculomotor axons terminate in the extraocular muscles and control eye movements, and the electromotor axons terminate in the electric organs. Also included in this complex are the **nucleus of Darkschewisch**, the **interstitial nucleus of Cajal**, and the **nucleus of the posterior commissure**. These nuclei are involved in the reflex control of the extraocular muscles that are controlled by the oculomotor nerve.

Coordination of Eye Muscle Action

As seen in Table 12-2, the effects of contraction of each of the individual eye muscles on eye movement is rather different. To produce the precise movements needed for the inspection and tracking of visual stimuli and to prevent fading of the retinal image, a very precise coordination of the activities of each of the eye muscle nuclei is required. This coordination is carried out by a system of neuronal groups: the reticular formation. Among the functions of the reticular formation is the coordination of the action of motor nuclei that innervate antagonistic muscles. The nuclei of Darkschewisch and Cajal are reticular formation nuclei that are specialized for coordinating the activities of the oculomotor nucleus with other nuclei of the brainstem, in particular, those of the vestibular system.

Coordination of the actions of eye muscles is also carried out by the reticular formation. An important pathway of the reticular formation is the **medial longitudinal fasciculus**, which consists of heavily myelinated axons and is a conspicuous feature of the dorsal brainstem. The reticular formation, the vestibular nuclei, and the nuclei of III, IV, and VI, are interconnected via this pathway.

EVOLUTIONARY PERSPECTIVE ON THE HINDBRAIN AND MIDBRAIN CRANIAL NERVES

The evolutionary development and organization of the cranial nerves of the hindbrain and midbrain have paralleled the evolutionary development of the head. The change from gill arches to jaws and hyoid arch as well as the later evolution of the muscular tongue in tetrapods were major adaptations. Other adaptations, such as the development of mechanisms for the lubrication and transport of food in the mouth and the ability to manipulate the air column in the mouth, throat, and body cavities or to use sonic or electromotor systems for communication between individuals, also permitted greater and more efficient survival and success of future generations. Still other adaptations involved the development and elaboration of the muscles of the eyes and the incorporation of jaw bones and muscles into the middle ear as devices to affect the conduction of sounds to the inner ear. All of these adaptations are reflected in the sensory and motor neuronal populations of the hindbrain and midbrain. Because nearly all of these structures operate in close coordination with one or more of the others, the midbrain–hindbrain region is a major zone for pathways involved in a large number of reflexes of the head and neck. In Chapter 13 on the reticular formation, which is another major component of the midbrain–hindbrain region, we shall see how these reflexes are coordinated and integrated with each other.

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13

The Reticular Formation

INTRODUCTION

Have you ever noticed that a person can speak at the same time as chewing a mouthful of food? Let us overlook the appallingly bad manners of such an act and consider instead how rarely such a person mistakenly bites his/her own tongue while happily chewing through the various other items that are in the mouth at the same moment. Consider what the tongue is doing during this process: not only is it manipulating the food to position it under the teeth for chewing and then transporting the chewed food back to the throat so that it can be swallowed, but it is also alternating these complex movements with the even more complex movements required for articulate speech (admittedly made less articulate by the presence of the food). What sort of neural system has taken notice of the location of the tongue, the position of the jaws, the states of contraction and relaxation of the flexor and extensor muscles that operate the jaws, and the muscles that control swallowing and respiration and other complex processes to permit these actions to occur as smoothly as they do?

The answer is the **reticular formation**, a neural system that has input from sensory and motor pathways that control central pattern generators for rhythmic motor patterns, such as respiration, swimming, walking, flying, the repetitive discharge of the electric organs in electric fishes, and chewing. In addition to providing these coordinating and organizing functions, the reticulobulbar and reticulospinal pathways are the principal routes of telencephalic control of voluntary movement of organs of the head and body in nearly all vertebrates, except mammals, where they work in close conjunction with the direct corticobulbar and corticospinal tracts. Regulation of

muscle tone (the degree of tension present in a muscle) is also a function of the reticular formation. These motor activities are regarded as the functions of the “descending” reticular formation.

The “ascending” reticular formation consists of those reticular pathways that ascend to the diencephalon and telencephalon. The functions of the ascending pathways are quite different from those of the descending reticular formation. The ascending functions of the reticular formation include processes such as sleep, dreaming, and arousal, as well as attention, which is the ability to filter out extraneous stimuli so that the animal can concentrate on the relevant stimulus. Of particular importance in the functioning of the reticular formation are the ascending serotonergic pathways and the noradrenergic pathways.

Much of the research on the ascending reticular formation has been done in mammals, partly for reasons of tradition, partly for convenience, and partly because human scientists can more readily identify (and identify with) states of arousal, wakefulness, attention, and so on, in mammals than they can in reptiles, amphibians, or fishes. Very good evidence does exist, however, for the presence of similar functions in non-mammalian amniotes and in anamniotes as well.

Despite its importance, the reticular formation is one of the more misunderstood and intimidating systems of the brain. To begin with, it has a formidable nomenclature that is rivaled only by the diencephalon in the variety and complexity of the names of its components. To make matters worse, different anatomists have used different systems of nomenclature that make the correspondences between vertebrate classes or even between relatively closely related species difficult for beginners to follow. Finally, the reticular formation is scattered through-

out the central nervous system from the spinal cord to the forebrain, which tends to obscure its overall organization.

Much of the difficulty in understanding the reticular formation comes from attempting to deal with the individual components of the mammalian reticular formation before having a clear appreciation of either the evolution of the reticular formation or of the overall structure and organization of the system as a whole. Once the general organization is understood in the context of a uniform nomenclature and in the light of the evolutionary development of the system, the individual components become manageable details that can be dealt with as needed. In this chapter, we will present the reticular formation in an evolutionary context and will show how its many components fit into a general pattern of organization, and we will attempt to make the nomenclature less intimidating and more consistent. We will also describe the relationship between the reticular formation and sensory, motor, and neurochemical systems. Finally, we will introduce some of the important functions of the reticular formation in the behavior of vertebrates.

THE ORGANIZATION OF THE RETICULAR FORMATION

The brainstem of vertebrates contains sensory nuclei of the cranial nerves (and their incoming sensory-root axons), the motor nuclei of the cranial nerves (and their outgoing motor-root axons), long ascending axons from the spinal cord, and long descending axons from the diencephalon and telencephalon. Interspersed among these are many clusters of neurons that are neither sensory nor motor. These clusters of neurons, which seem to fill in the spaces between the sensory and motor components of the brainstem, make up part of a coordinating system known as the reticular formation. The name is derived from the Latin word *reticulum*, which means a small net or mesh. Like the other great coordinating system, the limbic system, the reticular formation has strong connections with sensory systems, somatic motor systems, and visceral motor systems. We have already encountered the reticular formation in our discussions of ascending and descending pathways in the spinal cord; we have seen that reticulospinal pathways are a major route through which the brain controls movements of the body in all vertebrates and are the dominant route for the brain to control motor neurons in many of them, especially in most nonmammals. However, the functions of the reticular formation are far more pervasive than that and include roles in:

- The coordination of movements of the head and body by facilitation and inhibition of both voluntary and reflex movements.
- Alteration of respiration and blood pressure.
- Serving as a “gate” to block out sensory inputs, including pain.
- Psychological processes such as arousal and attention.

- Sleep and dreaming.
- Regulation of muscle tone.

Neurons of the Reticular Formation

Neurons of the reticular formation fall into three categories based on the size of the soma: small, large, and giant. At first glance they seem to be scattered throughout the tangle of dendrites and axons that make up the core of the medulla, pons, and midbrain apart from the compact sensory and motor nuclei of the cranial nerves and several other well-demarcated nuclear groups. A more careful examination will reveal, however, that the cell groups of the reticular formation indeed have an organization even though they are not arranged in neat packages with clear boundaries such as the cranial nerve nuclei. The overall organizational arrangement of the reticular formation is that of columns of cells arranged longitudinally along the length of the medulla, pons, and midbrain.

In general, the small cells comprise the lateral columns (**parvocellular** columns; “parvo-” = small), and the large and giant cells form more medial columns (**magnocellular** and **gigantocellular** columns; “magno-” = big and “giganto-” = giant). The gigantocellular cell columns also contain neurons of smaller size. The most medial column is the raphe column. Within these columns are subdivisions that can be distinguished according to cell size and type as well as their connections with other parts of the nervous system. Figure 13-1 is a schematic representation of the columnar organization of the reticular formation within the caudal brainstem (medulla and pons); several subdivisions are shown within each column. Although this simplified organizational scheme is generally satisfactory, you should be aware that some exceptions can be found.

The small-celled, lateral column tends to be the afferent zone of the reticular formation; these neurons receive axons from sensory systems of the brainstem and spinal cord as well

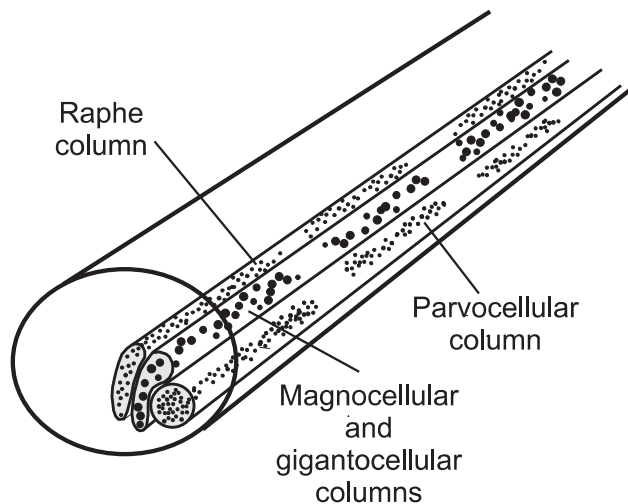


FIGURE 13-1. A schematic representation of the main cell columns of the reticular formation of the brainstem.

as from motor pathways. The more medial columns typically are the efferent divisions of the reticular formation; many of their axons descend to the motor neurons of the spinal cord and brainstem or ascend to higher levels of the nervous system.

Reticular formation neurons differ from neurons of cranial nerve sensory or motor nuclei in their cellular morphology. As shown in Figure 13-2, the dendrites of sensory or motor neurons of the cranial nerve nuclei tend to spread out like the branches of an oak or chestnut tree. The spread of these dendritic branches, however, remains within the sharply demarcated boundary of the nuclear group. In contrast, the dendrites of reticular neurons often are long and relatively straight. These dendrites tend to be of the isodendritic variety (see Chapter 2) and have a relatively consistent dorsal-ventral orientation within the brainstem. This dendritic pattern permits reticular neurons to be in contact with axons traversing the brainstem whether they rise dorsally from the ventral levels of the brainstem or descend ventrally from more dorsal portions.

The high frequency of isodendritic neurons in the reticular "core" of the mammalian brainstem led Ramon-Moliner and Nauta in the 1960s to speculate that the isodendritic pattern represents a primitive evolutionary condition from which more complex dendritic patterns evolved. Subsequent research on the reticular formation of lampreys, however, has revealed that while some divisions of the lamprey reticular formation possess the pattern of radially organized isodendrites, other divisions have a more dense dendritic organization than the mammalian pattern. These and other differences between lamprey reticular neurons and those of mammals suggest that the evolution of dendritic types may be a more complex story than a simple progression from an isodendritic organization to more complex and varied dendritic forms.

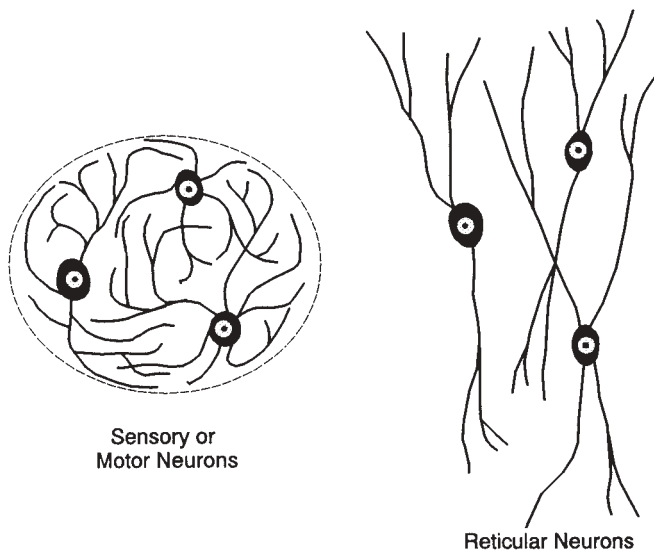


FIGURE 13-2. The arrangement of dendrites of reticular formation neurons is contrasted with the dendrites of sensory or motor neurons, which remain within the boundaries of their nuclear groups.

A characteristic of reticular neuron axons is that they are quite long and travel for considerable distances to other cell groups. In other words, they are Golgi Type I neurons. Inhibitory, Golgi Type II neurons are also a feature of reticular formation anatomy. In most vertebrate classes, reticular formation axons give off numerous collateral branches as they travel the length of the brainstem. An exception appears to be lampreys in which the long reticular axons do not have the characteristic collateralization. In addition to the long axons, shorter axons connect the individual subdivisions of the reticular formation so that the actions of these subdivisions are highly coordinated. Figure 13-3 illustrates a reticular neuron with long dorsoventrally oriented dendrites. An axon arises from the soma of this cell and bifurcates into two divisions that ascend and descend for long distances within the brainstem. As the axon travels its course, numerous collateral branches can be seen descending ventrally from it.

Giant Reticulospinal Neurons

Another characteristic of the reticular formation is the presence of giant neurons. In addition to the gigantocellular column, which contains neurons that are among the largest in the brainstem, the reticular formation of nontetrapods contains a relatively small number of neurons that have somata of enormous proportions. We have already encountered one of these in our discussion of the nontetrapod spinal cord, the Mauthner cell. Other giant cells may be scattered throughout the medulla, pons, and midbrain in various locations depending on the species of nontetrapod. These are the somata of the Müller cells. A common feature of these giant cells is that they send their axons to the spinal cord. The soma and dendrites of one such giant reticulospinal neuron from a larval lamprey are shown in Figure 13-4. The giant cells have their somata near the dorsal surface of the brainstem close to the floor of the ventricle. Their dendrites spread extensively in a ventral direction to the ventral margin of the brainstem where they intermingle with the passing axons of the ventral brainstem. Some dendrites occasionally cross the midline to the contralateral side.

These gigantic somata are associated with the giant axons of the spinal cord, which are involved in rapid evasion and escape responses. The principal advantage of a giant axon is its extremely short conduction time, because the speed of the

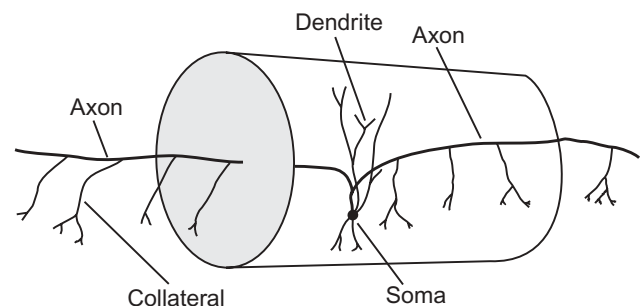


FIGURE 13-3. A reticular neuron with its long, bifurcated axon and many axon collaterals.

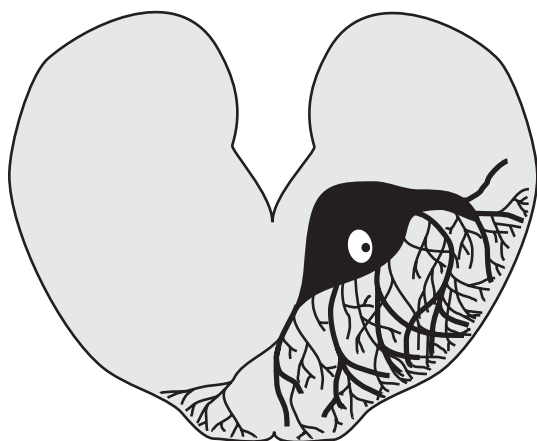


FIGURE 13-4. A giant reticulospinal neuron of a larval lamprey.

action potential increases as the axon diameter increases. As they emerge from their somata, the initial segments of these giant axons are much narrower in diameter than the rest of the giant axon. Although this narrower diameter of the initial segment results in a somewhat increased conduction time in that region, it does have the advantage of partially insulating the axon hillock from the giant axon. Without this partial insulation, the local membrane potentials on the axon hillock would leak out along the giant axon and thus the interplay of excitatory and inhibitory processes that determine whether or not an action potential is initiated in the axon hillock would be impaired.

Nomenclature of the Reticular Formation

One of the factors that complicates a comparative study of the reticular formation in various groups of vertebrates is the discrepancy in nomenclature used by different investigators. Early investigators of the reticular formation used variations on the nomenclature of J. B. Johnston and D. Tretjakoff in the first decade of the twentieth century to describe the reticular formation of nontetrapods; other anatomists preferred to apply the mammalian nomenclature used by Jerzy Olszewski (pronounced "Olshefsky") and Alf Brodal to name cell groups in nonmammalian reticular formations. The tendency in recent years has been to apply the Olszewski-Brodal nomenclature to nonmammals. The result has been a difficult situation for newcomers to the topic. Our approach to dealing with this problem has been to use the Johnston-Tretjakoff nomenclature for describing the agnathan reticular formation and the Olszewski-Brodal nomenclature for all other vertebrates. Table 13-1 shows these two nomenclatures. We recommend that you refer to the table frequently as you look at Figures 13-5, 13-6, and 13-9-13-11, which are schematic representations of the reticular formation in several representative vertebrates. The table will help you to see the location of each reticular component in the brainstem and the correspondence between the two nomenclatures.

Our treatment of the reticular formation has resulted in a simplification of certain details for the sake of clarity of pres-

TABLE 13-1. Nomenclatures of the Principal Components of the Reticular Formation of the Medulla, Pons, and Midbrain

Regions of Brainstem	Johnston-Tretjakoff Nomenclature ^a	Olszewski-Brodal Nomenclature ^a
Medulla	N. R. inferior	Raphe group
		N. R. gigantocellularis
		N. R. paragigantocellularis
		N. R. magnocellularis
		N. R. parvocellularis
		N. R. dorsalis
		N. R. ventralis
		N. R. lateralis
Pons	N. R. medius and N. R. superior	Raphe group
		N. R. pontis caudalis
		N. R. pontis oralis
		Locus coeruleus
		N. R. subcoeruleus
		N. R. tegmenti pontis
		N. R. pedunculopontinus
		Nucleus cuneiformis
Midbrain	N. R. mesencephali	Nucleus subcuneiformis
^a N. R. = Nucleus reticularis.		

entation. Our goal here, as elsewhere in this book, however, is not an exhaustive presentation of the reticular formation, for which we recommend the comprehensive work of Nieuwenhuys, ten Donkelaar, and Nicholson (1998), but rather to offer an introduction to the topic that gives the reader a framework onto which the specific details of any particular species easily can be attached.

The table shows the three regions of the brainstem that contain most of the reticular formation: the medulla, the pons, and the midbrain. Next, the components of the lamprey reticular formation in each brainstem region are presented in the Johnston-Tretjakoff nomenclature. Finally, the corresponding reticular formation components in jawed vertebrates, using the Olszewski-Brodal nomenclature, are presented. Keep in mind that one should not expect all components to be present in all classes of vertebrates or even within all species of a given class. These reticular components have evolved to perform certain specific functions in the adaptation of the animals to their own environments. Each species of a particular taxonomic group has its unique survival needs and adaptations to its environment, which may be somewhat different from those of their sister groups in a taxonomic organization. These differences are reflected in variations in reticular formation components.

The Reticular Formation of the Medulla, Pons, and Midbrain

Figures 13-5, 13-6 and 13-9-13-11 show schematic representations of the reticular formation of five representative vertebrates: a lamprey, a shark, a frog, a lizard, and a rat. Birds are not represented because of their similarity to reptiles. Amphibians pose a special problem because of the unique condition of their brainstem, in which many of the neurons have remained in their unmigrated positions close to the ventricles. This situation makes the recognition of individual neuronal groups, especially reticular neurons, difficult. Recent research on the brainstem of the northern leopard frog (*Rana pipiens*) has produced a detailed map of an amphibian reticular formation. The reticular formations of these animals have been chosen because they represent varying degrees of complexity and differentiation into specialized nuclei. We hasten to add that these reticular formations are not intended to represent an evolutionary sequence because lampreys and sharks evolved from separate lineages, modern amphibians were not derived from the amphibian lineage that gave rise to amniotes, and lizards evolved after mammals. Thus they represent an adaptive series rather than a phyletic series.

Figure 13-5 shows the brainstem of a lamprey with the components of the reticular formation in the Johnston-Tretjakoff nomenclature. Also shown is the location of the giant Mauthner cell body with its giant axon crossing the midline and descending to the spinal cord. The other giant cell bodies are not shown for the sake of simplicity of the diagram. One reticular cell group is shown in the medulla, the **nucleus reticularis inferior** (sometimes known as the **posterior rhombencephalic reticular nucleus**). In the caudal pons, at the level of the vestibular nerve, is the **nucleus reticularis medius** (sometimes known as the **middle rhombencephalic**

nucleus). More rostrally in the pons are two more reticular components that together make up the **nucleus reticularis superior** (sometimes known as the **anterior rhombencephalic reticular nucleus**). One component, located near the roots of the trigeminal nerve is known as the **trigeminal group**; the other, located near the isthmus (the narrow neck of the brainstem) is called the **isthmus group**. Finally, in the midbrain, or mesencephalon, is the **nucleus reticularis mesencephali**.

Compare Figure 13-5 with the reticular formation of a shark as shown in Figure 13-6. Note that a simple correspondence of the components of the reticular formations of the two animals is not easily made. In addition to the presence of the raphe group, the reticular nuclei of sharks (see also Fig. 13-7) contain a number of additional subdivisions and cell groups that give it considerably more in common with the reticular formation of amniotes than Figure 13-6 suggests. Another major difference is that the shark reticular formation has a more obvious longitudinal orientation than that of the lamprey. This can be seen in the most medial column, which has been labeled as the **raphe group**. The word "raphe" is derived from the Greek work meaning to "stitch" or "sew" and means a "seam" in biological terminology. The raphe column of neurons lies along the median "seam" that divides the right and left halves of the brainstem. The raphe group, as we have called it, actually consists of a series of separate neuronal populations with different cell types and connections, with such names as nucleus raphe dorsalis, nucleus raphe magnus, and nucleus raphe pallidus. Although no obvious raphe column is present in lampreys, scattered serotonin-containing neurons have been described in the lamprey brainstem that might serve as a rudimentary raphe system. As we will see later on in this chapter, serotonin is the major neuroactive substance of the raphe column.

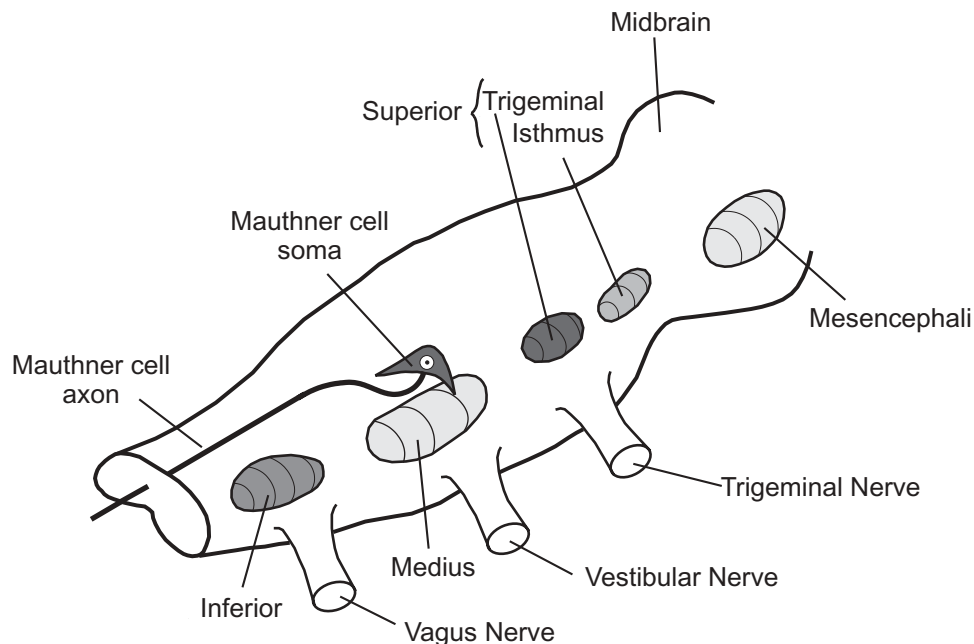


FIGURE 13-5. The main cell groups of the reticular formation of a lamprey.

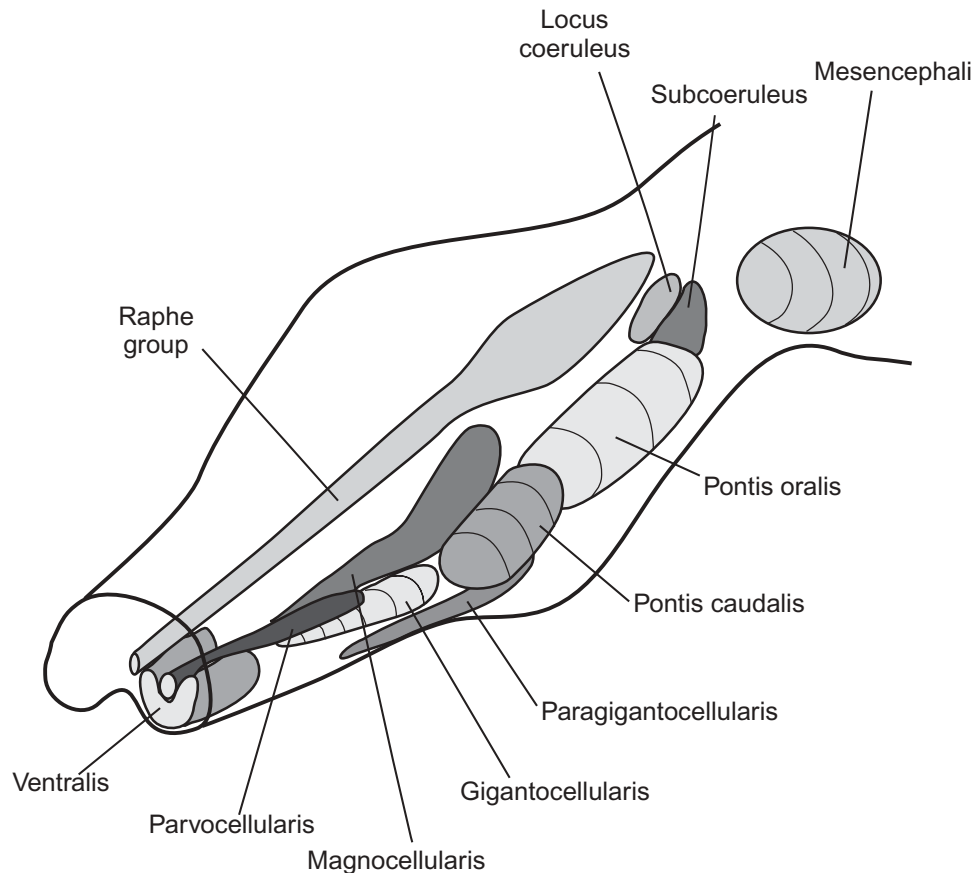


FIGURE 13-6. The main cell groups of the reticular formation of a shark.

For purposes of this introductory presentation, we have treated the raphe nuclei as a single entity, but the reader should be aware that further study of the reticular formation, and especially the chemical pathways within it, will require more detailed knowledge of the individual components of the raphe group. In general, axons from the caudal raphe nuclei project to the spinal cord while those of the rostral raphe nuclei project to other regions of the brainstem, the diencephalon, and the telencephalon.

With the aid of Table 13-1, the correspondences can be seen between the shark reticular formation in Figure 13-6 and that of the lamprey in Figure 13-5. Moving from caudal to rostral, we can see that the caudal levels of the raphe group, and the **nuclei reticularis parvocellularis**, **magnocellularis**, **gigantocellularis**, and **paragigantocellularis** of the shark, correspond to the nucleus reticularis inferior of the lamprey. These form the reticular formation of the medulla. Next, the middle and rostral levels of the raphe group as well as the **nuclei pontis caudalis** and **pontis oralis**, the **locus coeruleus** and the **nucleus subcoeruleus** of the pons of the shark correspond to the nuclei reticularis medius and reticularis superior of the lamprey. Finally, the nucleus reticularis mesencephali of the shark corresponds to the nucleus reticularis mesencephali of the lamprey.

Figure 13-8 is a drawing of a horizontal section through the hindbrain and midbrain of a goldfish and shows the arrange-

ment of reticulospinal neurons in longitudinal columns. The rostral end is at the top of the figure. The cluster of neurons labeled "n.mlf" (nucleus of the medial longitudinal fasciculus) is in the midbrain. The numbers RS1-RS7 indicate rhombomeres. The large, prominent objects located in RS4 are the lateral dendrites of the Mauthner cell. The rest of the Mauthner cell is out of the plane of the section. The giant Mauthner axons decussate and descend toward the spinal cord.

Figure 13-9 represents the reticular formation of a reptile, the tegu lizard. The correspondence between this animal's reticular formation and that of the shark shown in Figure 13-6 is rather straightforward. The raphe group extends the length of the brainstem to the midbrain. The parvocellular, magnocellular, gigantocellular, and paragigantocellular groups are present in the medulla. Pontis caudalis, pontis oralis, the locus coeruleus/subcoeruleus complex, and the **nucleus reticularis pedunculopontinus** are present in the pons, and the nucleus reticularis mesencephali is present in the midbrain. Despite the development of limbs in the tetrapod radiation, the reticular formation of nonmammalian amniotes does not differ significantly from that in fishes, although it is somewhat more complexly organized in birds than in reptiles. The reticular formation of alligators and crocodiles is more complex than that of other reptiles, which is consistent with their presumed closer evolutionary relationship to birds.

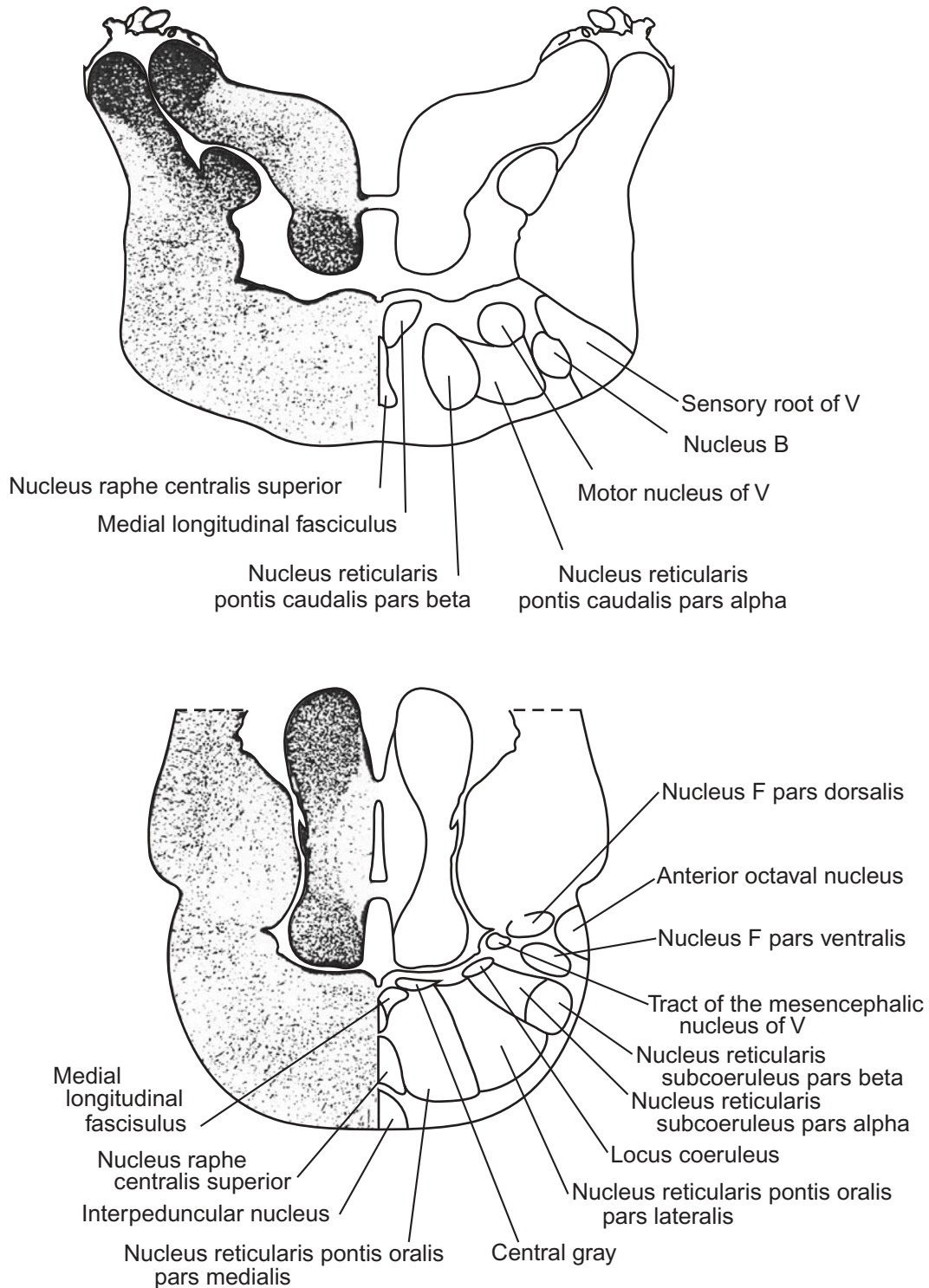


FIGURE 13-7. Transverse hemisections with mirror-image drawings through the reticular formation of the horn shark (*Heterodontus francisci*). The upper section is the more caudal. Adapted from Cruce et al. (1999) and used with permission of John Wiley & Sons.

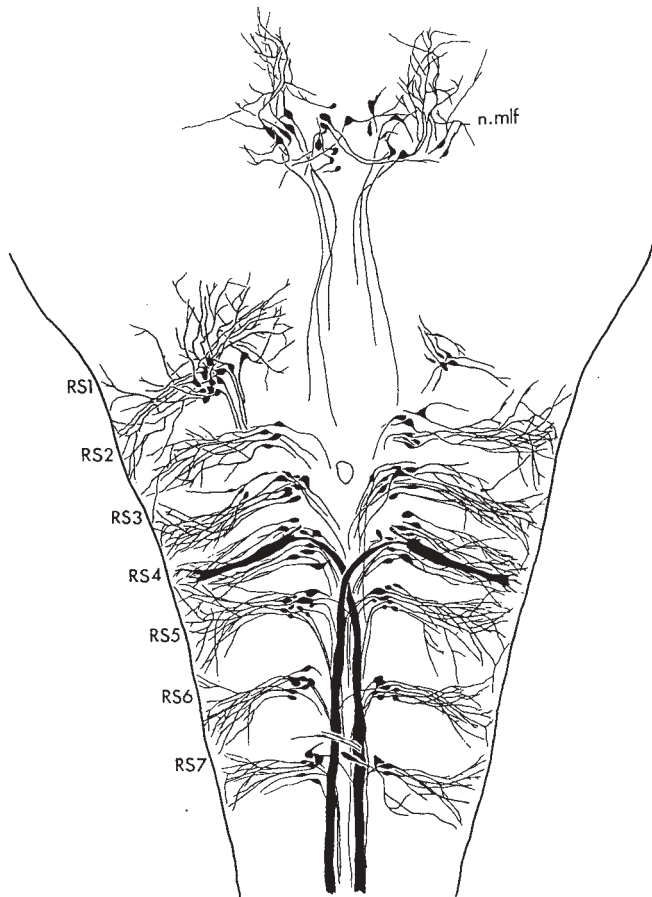


FIGURE 13-8. Drawing of a horizontal section through the hind-brain and midbrain of a goldfish showing the arrangement of reticulospinal neurons into longitudinal columns. Top is rostral. The numbers RS1–RS7 indicate rhombomeres. The large objects in RS4 are the lateral dendrites of the Mauthner cells. The giant Mauthner axons can be seen crossing the midline and descending toward the spinal cord. From Lee et al. (1993) and used with permission of John Wiley & Sons.

Figure 13-10 is a reconstruction of the hindbrain of the northern leopard frog to show its reticular formation. The similarity of this animal's reticular formation to that of the tegu lizard and that of the rat shown in Figure 13-11 is impressive. In the medulla, the dorsal and ventral reticular nuclei are present as well as the parvocellular, magnocellular, gigantocellular, and paragigantocellular cell columns. The raphe column is present as well. Rostral to the raphe is the locus coeruleus and nucleus subcoeruleus. The nucleus reticularis pontis caudalis is situated close to the junction of the medulla and pons. Rostrally, in the same cell column, is the nucleus reticularis pontis oralis as well as a pontis oralis medialis and a pontis oralis lateralis. Finally, near the pontomesencephalic junction are the nucleus cuneiformis and the nucleus subcuneiformis.

When we look at the mammalian reticular formation in Figure 13-11, which is represented by the reticular formation of a rat, we see a number of additional reticular formation components. Serial transverse sections of the reticular formation of

a rat are also shown in Figure 13-12 for comparison with Figure 13-11. More than 30 components of the mammalian reticular formation have been described thus far, and the list is probably not yet complete. Part of this apparent increase in components may be only a reflection of the fact that the mammalian reticular formation has been far more intensively studied than that of any other class of vertebrates. Such detailed examination of a neural system invariably results in the recognition of new components and the division of formerly recognized components into subcomponents, each with a separate name. Indeed, our simplified treatment of the reticular formation has glossed over a number of such subdivisions in nonmammals as well. One could suppose that after a more detailed examination of the reticular formation of nonmammals, especially with the use of the new, sophisticated tools now available, many more reticular components would emerge. The recent detailed description of the frog reticular formation may be a case in point. On the other hand, some mammals possess certain characteristics not frequently found in other tetrapods, particularly the ability to use the digits of the limbs as organs to manipulate objects in the environment. To be sure, some reptiles perform manipulatory movements with their forelimbs, such as digging and scratching, but more often than not, the snout is the principal organ for manipulation of objects. The same applies to birds. Many mammals, however, have developed the digits of the forelimbs into highly dexterous organs that can hold and turn objects for inspection and feeding or that can pull, lift, bend, or otherwise manipulate objects. Many primates and some birds have adapted their hindlimb digits as very sophisticated devices for grasping.

Despite the greater complexity of the rat reticular formation, we can see that the basic pattern remains. The raphe group is present as the medial-most column, although the **nucleus reticularis paramedianus** has been added adjacent to it. The by-now-familiar parvocellular, magnocellular, gigantocellular, and paragigantocellular groups are present in the medulla, although paragigantocellularis now is seen as two divisions, a dorsal division adjacent to the raphe-group column and a lateral division that lies ventral to parvocellularis. Also present in the medullary reticular formation at its caudal end are the **nucleus reticularis ventralis**, **nucleus reticularis dorsalis**, and **nucleus reticularis lateralis**. Moving rostrally into the pons, we find nucleus reticularis pontis caudalis and nucleus reticularis pontis oralis in their familiar locations along with the locus coeruleus and the now, much enlarged nucleus subcoeruleus. At the level of the isthmus (the junction of the pons and the midbrain), we find the nucleus reticularis pedunculo-pontinus, which consists of two subdivisions, a compact part (**pars compacta**) and a dispersed part (**pars disseminata**). At the rostral end, the mesencephalic reticular formation consists of the cuneiformis-subcuneiformis complex.

The Reticular Formation of the Diencephalon

The most rostral extension of the reticular formation is the **nucleus reticularis thalami** (and see Chapter 19). In mammals, where it has been most extensively studied, this nucleus is a thin sheet of neurons that sits like a cloak over the dorsal thalamus at its rostral end. Its cells are characteristic of reticular neurons elsewhere in the brainstem; its axons project

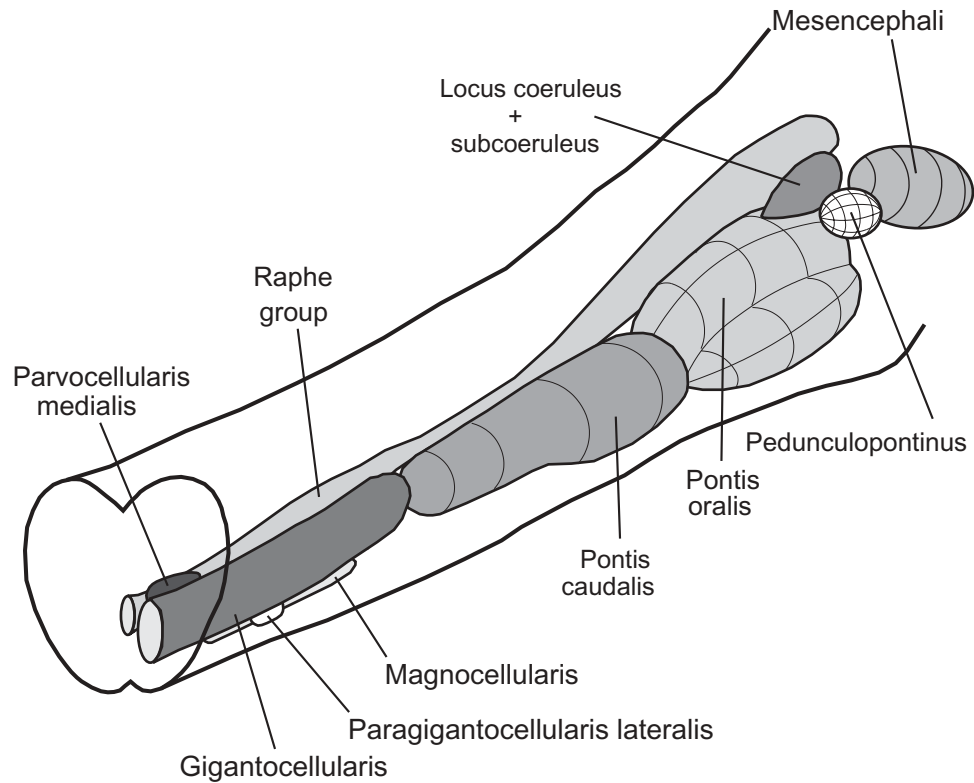


FIGURE 13-9. The main cell groups of the reticular formation of a lizard.

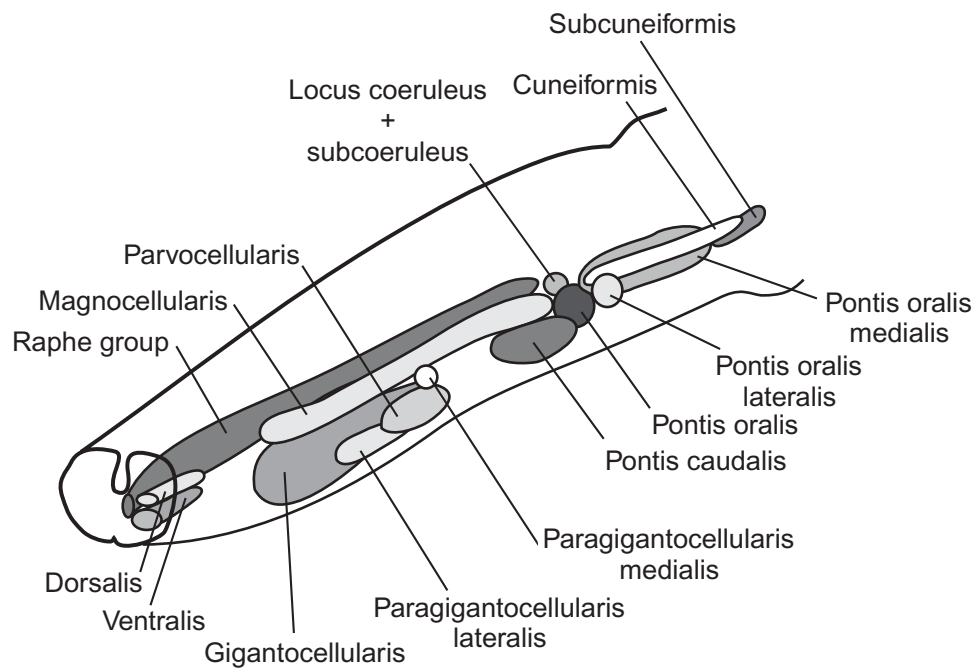


FIGURE 13-10. The main cell groups of the reticular formation of a frog. Based on Adli et al. (1999) and used with permission of John Wiley & Sons.

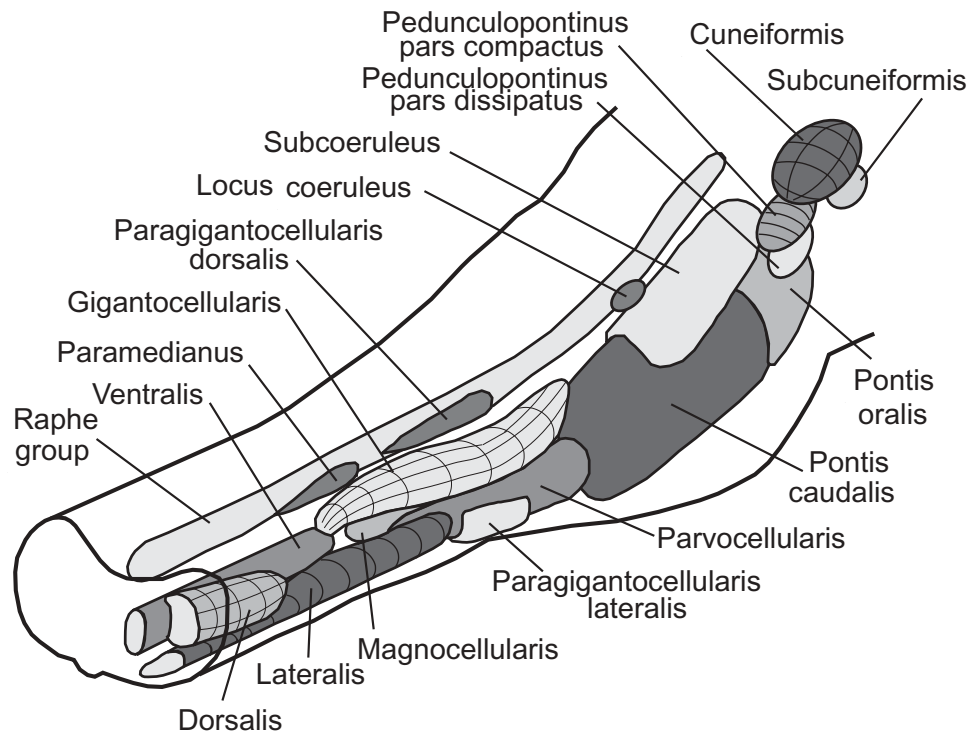


FIGURE 13-11. The main cell groups of the reticular formation of a rat.

widely to other thalamic nuclei, and its dendrites receive collaterals of the axons that interconnect the dorsal thalamus and the cerebral cortex. The thalamic reticular nucleus also receives fibers from the striatum and basal forebrain of the telencephalon, from the substantia nigra in the mesencephalon, and from the raphe nuclei, pedunculopontine nuclei, and the locus coeruleus of the reticular formation. These axonal inputs to the nucleus also can be characterized by the neurotransmitters that are present in their terminals: acetylcholine, GABA, serotonin, and norepinephrine. Nuclei in the diencephalon with at least some of these properties have been described in all vertebrate classes, suggesting that the thalamic components of the reticular formation, like their medullary, pontine, and mesencephalic counterparts, are part of a phylogenetically old and relatively stable system. The thalamic reticular nucleus is thought to play a role in generating the slow oscillatory electrical rhythms observed in the thalamus and cerebrum during slow-wave sleep.

PATHWAYS OF THE RETICULAR FORMATION

In all vertebrates, the descending pathways from the reticular formation are important for the brain's ability to control movements of the musculoskeletal system and the specialized organs of the head, such as the jaws and eyes, especially for voluntary movement. When limbs are present, these too are controlled by descending reticular formation pathways. The pathways from the reticular formation to the spinal cord, for

control of limb and trunk musculature, are called **reticulospinal** pathways; those descending reticular formation pathways that end on cranial nerve motor nuclei in the brainstem are known as **reticulobulbar** pathways. In addition to reticulospinal and reticulobulbar control of their motor neurons, mammals and birds have corticospinal and corticobulbar pathways that work together with the descending reticular pathways to provide voluntary control over the musculoskeletal systems of the head and body. Indeed, in nonmammals, the reticulospinal and reticulobulbar pathways constitute the bulk of all the descending pathways in the brainstem and spinal cord.

Contemporary studies of the reticular formation of nonmammals have revealed a pattern of descending pathways that is remarkably consistent among the vertebrate classes, including mammals. This suggests that once we make allowances for the reticular formation specializations associated with the development of limb locomotion and the development of highly dexterous digits on the limbs of some mammals, the reticular formation emerges as one of the more conservative and stable of the neuronal systems.

The principal sources of descending pathways are from the reticular nuclei pontis caudalis, pontis oralis, parvocellularis, magnocellularis, and gigantocellularis. The descending axons from these nuclear groups travel primarily in the **medial longitudinal fasciculus**, which is one of the main highways of the reticular formation. In mallard ducks, part of the parvocellular and gigantocellular reticular formation areas give rise to projections to a nucleus that lies in the rostral spinal cord and caudal brainstem, called the **supraspinal nucleus** (see Chapter 12). This nucleus is a rostral extension of the ventral horn of the spinal cord, and it innervates the extremely

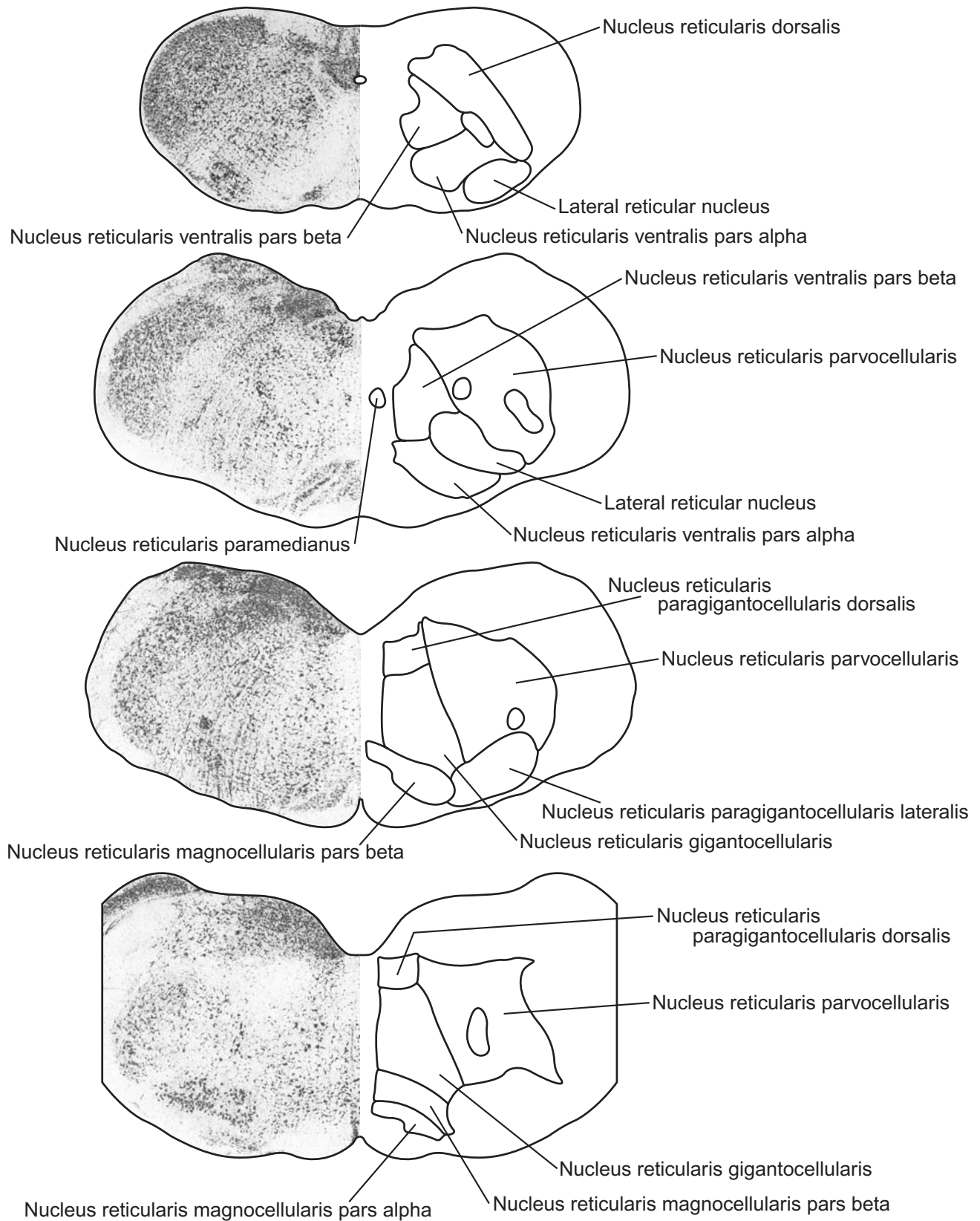


FIGURE 13-12. Transverse hemisections with mirror-image drawings through the reticular formation of a rat. Adapted from Newman (1985) and used with permission of the Akademie Verlag.

complex neck musculature (involving 16 cervical vertebrae and over 200 muscle slips) that is used to position the head for feeding, drinking, preening, and other activities. In conjunction with innervation of jaw and tongue motor nuclei, the reticular formation thus plays an important role in the coordination of all of the muscle groups used in feeding and other complex behaviors that utilize head musculature. In other animals, the reticular formation likewise serves to coordinate many complex motor functions of both the head and the body. Additional descending pathways of the reticular formation originate in the locus coeruleus-subcoeruleus complex and portions of the raphe group. These descending reticular projections typically travel in the lateral and ventral funiculi of the spinal cord.

In addition to its connections with the motor neuron pools of the brainstem and spinal cord, the reticular formation also has connections with the cerebellum, the diencephalon, and a number of structures within the telencephalon, including the cerebral cortex in mammals. These connections generally are via the **central tegmental bundle**, as well as the medial longitudinal fasciculus and the dorsal tegmental and nigrostriatal bundles. These pathways will be discussed below and in subsequent chapters

Chemical Pathways of the Reticular Formation

In addition to being classified according to the locations of their target neuronal populations, reticular formation pathways can also be classified according to the neurotransmitters that are produced in their somata. These include norepinephrine, epinephrine, serotonin, acetylcholine, GABA, and several others, although the primary neurotransmitters of many reticular formation pathways are unknown at present. In addition to neurotransmitters, many of these neurons also contain neuropeptides and other neuroactive substances that modulate the action of the transmitters in a variety of ways. Many of the pathways are ascending, although some descend to the spinal cord as well. Figures 13-13-13-16 summarize these chemically defined pathways based largely on the mammalian literature, which has been the most intensively studied. Given the general stability of the reticular formation during vertebrate evolution, the figures tell a reasonably accurate story for vertebrates as a whole.

Early investigators of the chemically defined pathways originally referred to the cell groups of origin of these axons by letters of the alphabet: A and B. The A cell groups contain catecholamines, and the B groups contain serotonin. Although virtually all of these groups have now been associated with specific, named aggregations of neurons in the brainstem, the A and B designations still appear frequently in the literature, and the serious student of this topic should become familiar with them. In Figures 13-13-13-15, we present these catecholaminergic and serotonergic pathways with both the names and the A or B designations of their cells' origin. In these three figures, some details have been simplified for clarity in an introductory presentation. Thus, not all cell groups or all of their connections are shown.

Figure 13-13 summarizes the pathways that have been characterized by the presence of the neurotransmitter norepinephrine and/or epinephrine. Because another name for

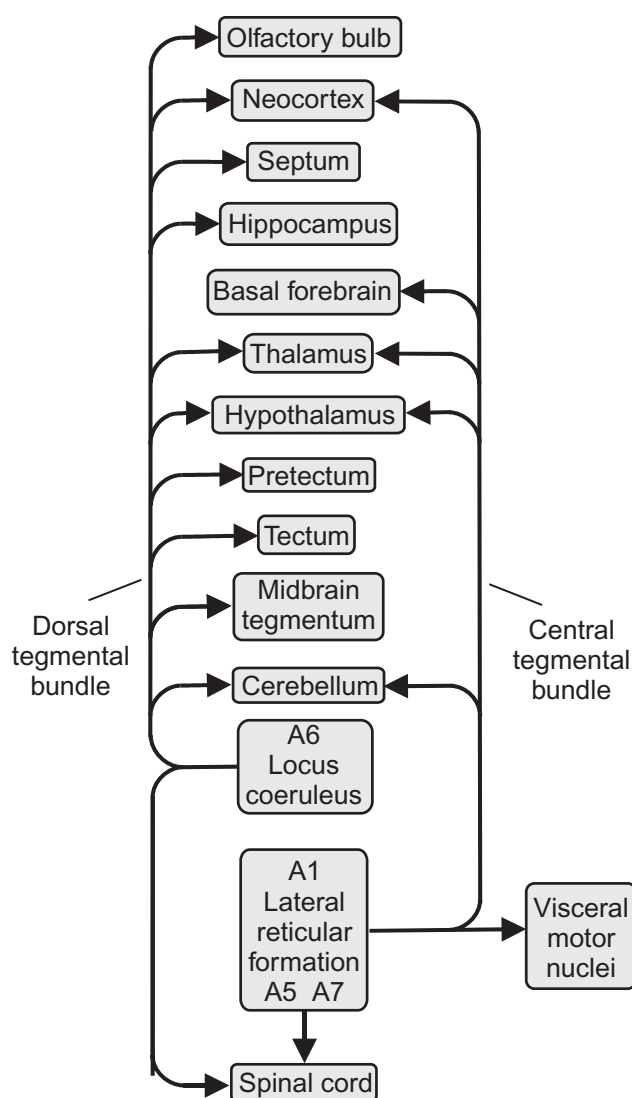


FIGURE 13-13. A summary of the main noradrenergic pathways.

norepinephrine is noradrenaline, these pathways are often referred to as “noradrenergic” pathways. The figure shows two noradrenergic pathways: one, on the left, originating in the locus coeruleus, and a second, on the right, that originates in catecholamine cell groups within the lateral reticular formation. Both pathways also have descending components to the spinal cord; the lateral reticular pathway also sends fibers to the visceral motor nuclei of the brainstem such as the motor nucleus of the vagus nerve. The locus coeruleus pathway ascends in the **dorsal tegmental bundle** and sends its axon terminations to a wide variety of target neurons, including the cerebellum, the mesencephalon (tegmentum and tectum), the diencephalon (pretectum, hypothalamus, and thalamus), and the telencephalon (septal nuclei, hippocampus, olfactory bulb, and cerebral cortex). The lateral reticular pathway's projections, by way of the **central tegmental bundle** (sometimes known as the **ventral noradrenergic bundle**), are more limited and include the cerebellum, thalamus, hypothalamus,

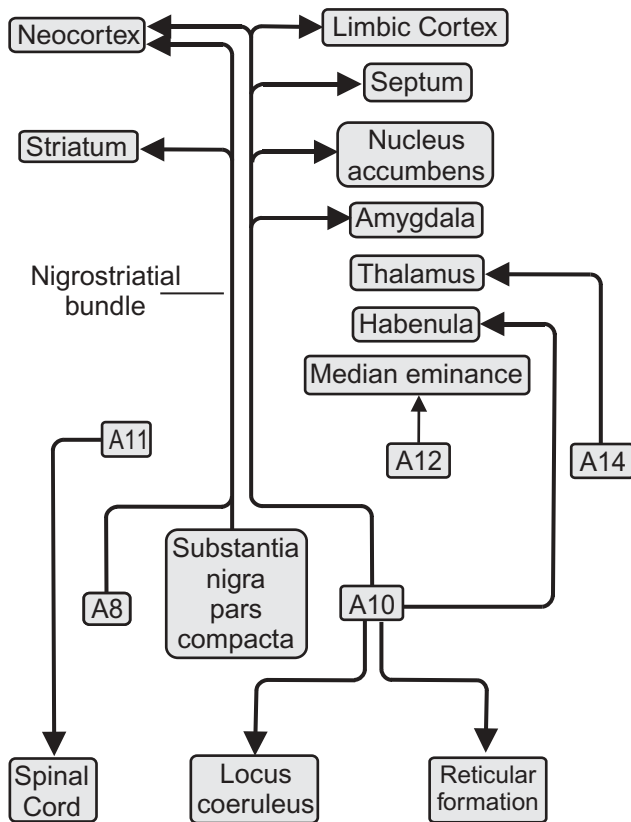


FIGURE 13-14. A summary of the main dopaminergic pathways of the midbrain and hypothalamus.

basal forebrain, and neocortex. The central tegmental bundle should not be confused with the **central tegmental tract**, which is more medially located and consists of ascending axons from the large-celled, medial reticular formation that terminate in the thalamus. The central tegmental tract is part of the ascending reticular formation. The neurotransmitters of this system are largely unknown, although one group, axons originating in the pars compacta of the nucleus reticularis pedunculopontinus, utilizes acetylcholine.

Figure 13-14 schematically illustrates two dopaminergic pathways: a midbrain-originating pathway from the A8, A9, and A10 cell groups and a hypothalamus-originating pathway from A11, A12, and A14. The midbrain group consists of two main cell populations: (1) the A8 and A9 group, which project mainly to the corpus striatum in the depths of the telencephalon, and (2) the A10 group, which is the source of a major projection to the limbic system including the habenula, septal nuclei, nucleus accumbens, limbic cortex, and amygdala. The A10 group (sometimes known as the **ventral tegmental area**) also has projections to the locus coeruleus and brainstem reticular formation. Because of its strong connections to the limbic system, the ascending dopaminergic pathway from the A10 group is known as the **mesolimbic pathway** (from mesencephalon to the limbic system). This pathway is thought to play a role in pleasure and reward mechanisms and may be related to drug addiction.

The dopaminergic cell groups of the tegmentum will be dealt with in detail in Chapter 17. The A8 cell group also is known as the **retrosubstantia nigra** ("behind" the red nucleus). The A10 group, or ventral tegmental area, consists of scattered cells in the medial part of the ventral tegmentum. The A9 group is a subdivision of the **substantia nigra**, which is a prominent feature of the midbrain tegmentum of mammals and has been reported in various nonmammals as well. This particular subdivision of the substantia nigra is known as the **pars compacta** (compact part). The substantia nigra also contains a division known as the **pars reticulata** (the mesh-like part), which we will encounter shortly in connection with a different chemically defined pathway. The A8 and A9 groups are the source of a major ascending, chemically defined pathway to the telencephalon known as the **nigrostriatal bundle**, because one of its principal targets is the dorsal striatum. This pathway also is known as the **mesostriatal dopaminergic pathway** (mesencephalon to striatum). Degeneration of the dopamine-producing neurons in the substantia nigra has been associated with the motor disorder known as Parkinson's disease.

The A11, A12, and A14 cell groups are the hypothalamic component of the dopaminergic pathways. These are scattered throughout the hypothalamus and around the third ventricle. The A11 group sends fibers to the spinal cord and the A14 group to the thalamus. The A12 group sends its axons to the **median eminence** of the hypothalamus, which is the transition zone between the hypothalamus and the posterior pituitary.

Figure 13-15 diagrams some of the B cell groups that make up sources of the **serotonergic pathways**. Many of these B groups are components of the raphe-group cell column. For example, the B5, B6, B7, B8, and B9 groups are in the rostral end of the raphe-group column. These groups have widespread projections that include the substantia nigra, neocortex, striatum, and such limbic structures as the hypothalamus, amygdala, septum, and hippocampus. The B1, B2, B3, and B4 groups comprise the caudal end of the raphe-group column. They send their axons to the cerebellum and the spinal cord.

Finally, in Figure 13-16, we find pathways emanating from the pars reticulata of the substantia nigra. The neurons of the pars reticulata produce the inhibitory neurotransmitter GABA. The targets of these GABA-ergic pathways include the parvocellular components of the reticular formation, which participate in control of muscles of the mouth and face region, the tectum of the midbrain, and various cell groups in the thalamus. GABA-ergic neurons also are in nucleus reticularis magnocellularis, which projects to the spinal cord and mediates loss of muscle tone during sleep, and the thalamic reticular nucleus (not shown in the figure).

The chemical pathways of the reticular formation play a role in many neural processes. For example, the ascending serotonergic and noradrenergic pathways play a role in sleep and wakefulness. The descending noradrenergic pathways function in the integration of the activities of the sympathetic nervous system, especially heart rate and blood pressure, via the preganglionic neurons in the intermediolateral column of the spinal cord, the nucleus solitarius, and the dorsal motor nucleus of the vagus nerve. The dopamine pathways are involved in the mechanisms of voluntary movement. In addi-

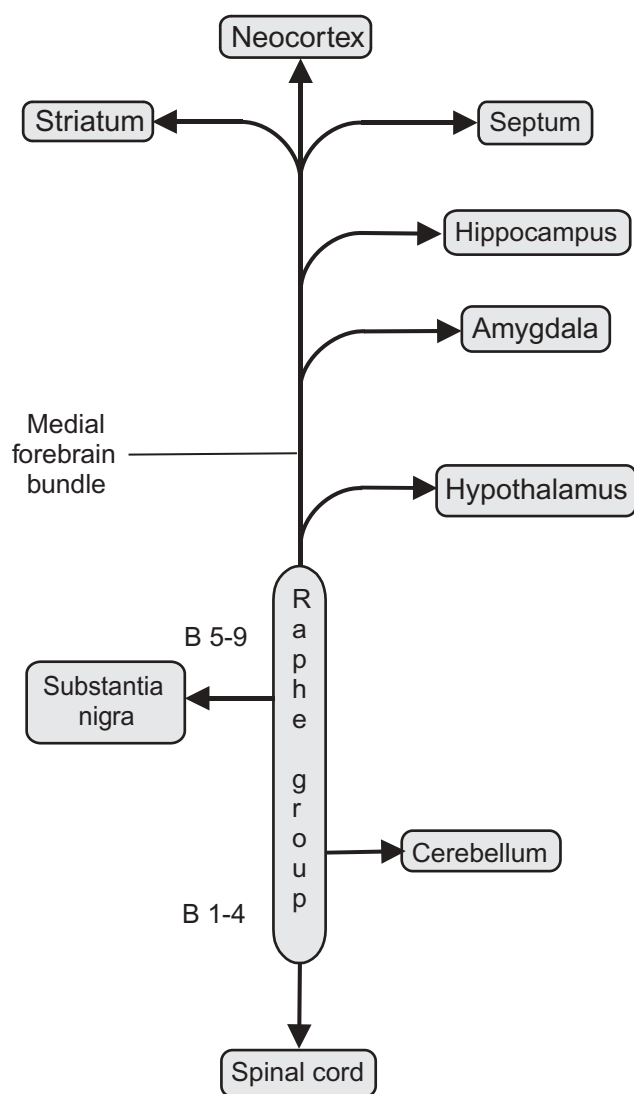


FIGURE 13-15. A summary of the main serotoninergetic pathways.

tion, many of the exogenous chemical compounds that have stimulating effects on behavior have been found to act on receptor sites in the dopamine system.

THE RETICULAR FORMATION AND SLEEP

Among the functions of the ascending reticular formation is the control of sleep and wakefulness. Although the adaptive value and functions of sleep are not yet fully understood, one thing is clear; rather than being a shutting down of the nervous system, sleep is an active process. Sleep does play a restorative role, but for many vertebrates it also is an important behavioral adaptation that keeps them inactive at the very time of day or night that many of their predators are searching for prey.

In marsupial and placental mammals, sleep occurs in several phases that can be distinguished by recording electroencephalograms (EEGs) as the subject passes from wake-

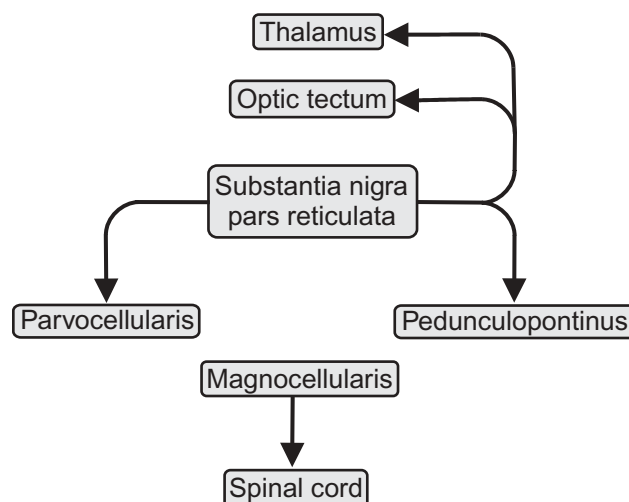


FIGURE 13-16. A summary of the main GABAergic pathways.

fulness to sleep and back again. Two major types of sleep have been noted: **slow-wave sleep (SWS)**, characterized by low-frequency, high-voltage EEG waves, and **fast-wave sleep (FWS)**, which consists of high-frequency, low-voltage waves. Because EEGs recorded during FWS resemble waking EEGs and yet occur during very deep sleep, FWS is also known as *paradoxical sleep*. Another feature of FWS is the occurrence of occasional jerks of the head, neck, limbs, or whole body, as well as rapid eye movements (**REMs**). FWS, therefore, is often known as **REM sleep**. Humans who have been awakened during FWS, often report dreaming. FWS seems to be a phenomenon limited to amniotes, many of which also show REMs and other motor signs associated with dreaming. Since dreams are private mental events, only humans with appropriate language can report that they were dreaming.

A number of components of the ascending reticular formation have been found to play a role in sleep and wakefulness. The pontine and midbrain levels of the reticular formation have been the subject of considerable attention by neuroscientists. Among these are the **parvocellular**, **magnocellular**, and **gigantocellular** cell columns. In recent years, however, particular attention has been focused on the **pontis oralis**; the rostral **raphe**, the **locus coeruleus**, the nucleus **pedunculopontinus**, and the **parabrachial nuclei** also have been found to play critical roles. Pontis oralis contains neurons that project to the oculomotor, trochlear, and abducens nuclei to produce the REMs, as well as to motor neurons in the ventral horn of the spinal cord that produce the muscles twitches that often occur during sleep. Other cells in pontis oralis orchestrate the loss of muscle tone that is typical of REM (rapid-eye movement) sleep. SWS (slow-wave sleep) results, in part, from rhythmic firing of thalamocortical neurons. Their rhythmicity is driven by cells of the **nucleus reticularis thalami**.

The pattern of high-frequency, low-voltage EEG waves that accompany FWS may have evolved more recently than the origin of the synapsid line to mammals, since monotreme sleep differs in some of its features. In the platypus, REM sleep does occur, as evinced by the movements of the eyes in addition to twitching of the body. In fact, the platypus spends more of its sleep period in the REM state than any other mammal.

BOX 13-I. Neuroactive Substances and Sleep

Several neurotransmitter and neuropeptide systems have been implicated in sleep and wakefulness:

- **Acetylcholine:** Injections of a cholinergic agonist into pontis oralis results in FWS.
- **Glutamate:** Glutamatergic REM-inducing cells in pontis oralis are inhibited by serotonergic, noradrenergic, and possibly dopaminergic inputs.
- **Serotonin:** The main source of serotonin in pontis oralis is from the dorsal and ventral tegmental gray matter. Although the raphe nuclei are a major source of serotonin to the neo-cortex and other regions, they do not appear to project to pontis oralis. Serotonin release from the pontine raphe does, however, diminish during REM sleep.
- **GABA:** Increases in GABA in pontis oralis induce wakefulness; decreases in GABA produce REM sleep. GABA also inhibits the serotonin-producing cells in the pontine raphe. The thalamic reticular nucleus contains large amounts of GABA, which plays an important role in the changes in the rhythmic activity of thalamocortical pathways that is reflected in EEG recordings during sleep and wakefulness.
- **Noradrenaline:** Noradrenergic cells from the locus coeruleus project to pontis oralis, as well as to thalamus and cortex.
- **Histamine:** Histaminergic neurons from the tuberomammillary nucleus of the posterior hypothalamus pass to the pontine reticular formation. Histaminergic neurons are believed to promote wakefulness and the general level of arousal.

Several neuropeptides have also been implicated in sleep and wakefulness. One of these, **corticotatin**, which is similar in structure to somatostatin and binds to somatostatin receptors, induces sleep. A second neuropeptide is **orexin**, which is also called **hypocretin**. Orexin innervates neurons that produce a number of neurotransmitters involved in sleep, such as dopamine, histamine, acetylcholine, and serotonin. A number of animal experiments have suggested that orexin may be an effective treatment for human narcolepsy.

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However, during the REM sleep state, the electroencephalogram is of moderate to high voltage, rather than the low voltage state seen in marsupial and placental mammals. This low-voltage shift during REM sleep may thus be a more recent adaptation, as well as its relatively shorter duration.

Interestingly, echidnas have a different pattern that may have uniquely evolved in their taxon in conjunction with their

relatively more vulnerable situation during sleep, since they do not sleep in protective burrows as the platypus does. During their sleep state, the discharge patterns of their reticular formation neurons remain asynchronous. Echidna can be aroused from their sleep state with relatively minor touches, and they do not evince the twitching movements seen in the platypus and in marsupial and placental mammals.

Among the ascending pathways of the spinal cord is the spinoreticular tract, which arises from the dorsal horn and terminates in the reticular nuclei gigantocellularis and lateralis in the medulla and pontis caudalis in the pons. This pathway plays a role in the modulation of sensory-motor activities of the body. It also is one of the ascending pathways that carries information about pain. A recent study of the responsiveness of axons of the spinoreticular tract to pain stimuli in sleeping cats revealed that the spike activity of these units was unaltered during SWS. During FWS (fast-wave sleep), however, the units showed a marked reduction in responsiveness to pain.

Figure 13-17 is a schematic representation of some of the cell groups and pathways of the reticular formation that play a role in sleep and wakefulness. The thalamus and cortex are influenced by two major pathways. One arises in pontis caudalis, pontis oralis, and gigantocellularis and the other originates in the locus coeruleus, dorsal raphe, and parabrachial nuclei. These pathways control the thalamocortical cycles of excitation and inhibition that result in the various types of EEG patterns seen during sleep and wakefulness. In addition, these nuclei give rise to descending components that affect the changes in muscle tone that occur during different sleep stages as well as muscle twitches that occur during sleep. Finally,

pontis oralis affects the activity in the eye muscles by a direct pathway to the oculomotor, trochlear, and abducens nuclei and also by an indirect route via the vestibular nuclei to these same eye-muscle nuclei. These pathways produce the REMs that occur during fast-wave sleep.

EVOLUTIONARY PERSPECTIVE ON THE RETICULAR FORMATION

The reticular formation has been rather conservative in its evolution. In virtually all jawed vertebrates, one can readily recognize the main components of this system: the raphe group spanning the length of the hindbrain, the parvocellular, magnocellular, and gigantocellular groups of the medulla, the pontis caudalis and pontis oralis group of the pons, the locus coeruleus, and the midbrain reticular formation. The development of limbs has been accompanied by the gain of certain additional components in tetrapods; further structures have evolved in mammals and birds along with their more elaborate use of limbs and digits. Similarly, the chemical pathways have been relatively conservative in their evolution.

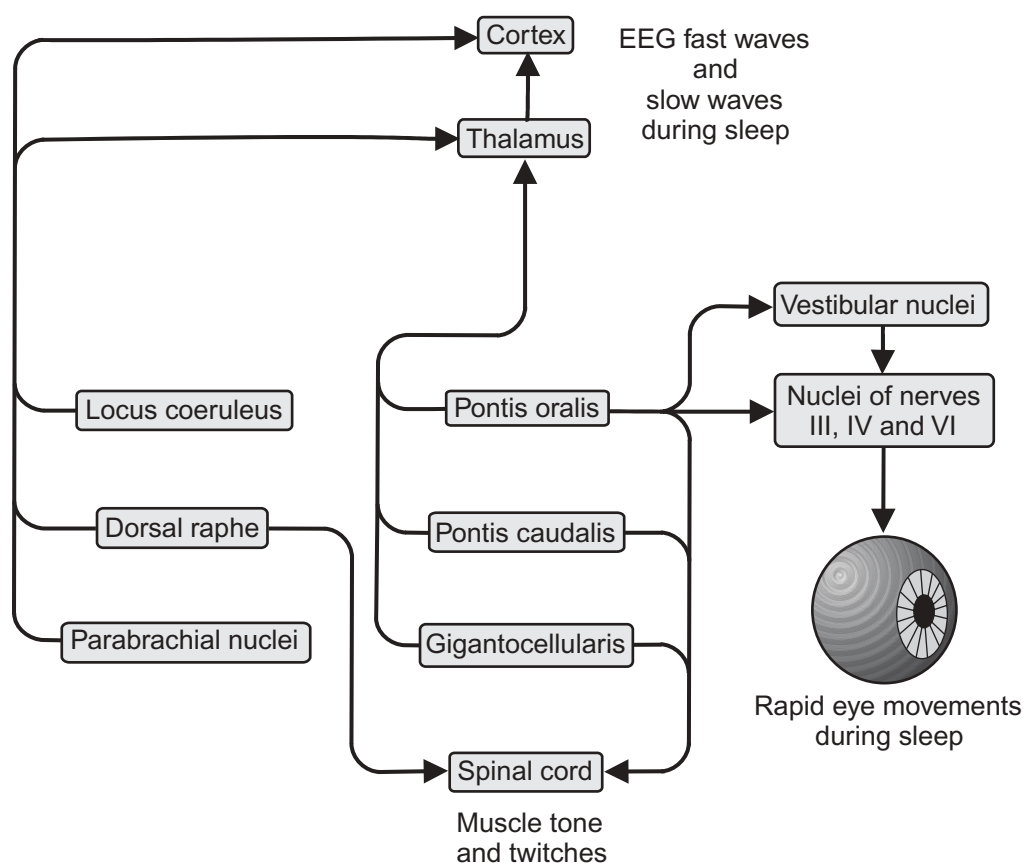


FIGURE 13-17. Some of the main cell groups and pathways of the mammalian reticular formation that are involved in sleep and dreaming.

BOX 13-2. Constant Vigilance and Unihemispheric Sleep

In Greek mythology, Hera, the queen of the gods, employed a watchman named Argus, who had 100 eyes. Because only a few of his eyes slept at any one time, Argus could stay on constant guard day and night. Today, we smile at the fantastic concept of this myth; however, for some animal species, the notion of one eye sleeping while the other stands guard is a reality. These species display a phenomenon known as **monocular sleep**, in which one eye is open and the other is closed. The open eye is fully responsive to events in the visual world even though the animal appears to be asleep. The observation of monocular sleep has been made in many avian species, in cetaceans (whales and porpoises), Otariidae (eared seals, including the fur seals and sea lions), Sirenia (manatees), and possibly in some reptiles.

We know today that it is the brain that sleeps and not the eyes. When sleep occurs, it generally is a bilateral phenomenon; i.e., a high coherence is observed between the patterns of electrical activity that are associated with sleep in the two cerebral hemispheres. Sleep comes at a price, however—a greatly diminished ability to survey the environment for predators or other sources of danger. Presumably in response to this inherent disadvantage, some species have evolved the ability to sleep with one only cerebral hemisphere while remaining awake with the other. This phenomenon is known as **unihemispheric sleep**.

The form of sleep that occurs in unihemispheric sleep is slow-wave sleep (SWS). On the other hand, in bihemispheric sleep, when both eyes are closed, electrical recordings from the two hemispheres show not only SWS but also fast-wave sleep, rapid eye movements, and a loss of muscle tone.

The independence of the two hemispheres for sleep in these animals is further attested to by a study of unihemispheric sleep deprivation in bottlenose dolphins. When one hemisphere was deprived of sleep, only that hemisphere showed a sleep rebound during recovery sleep. That monoc-

ular sleep is related to predator defense is supported by the observation that, when sleeping in a group, mallard ducks at the periphery of the group show more unilateral SWS than do the birds at the center. Moreover, the open eye of a bird that is on the periphery of the group typically is the one that faces away from the group.

If the ancient Greeks had known about unihemispheric sleep, perhaps Argus might have needed only 2 eyes instead of 100.

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14

The Cerebellum

INTRODUCTION

An inspection of the gross anatomy of an avian or mammalian brain reveals two major masses of tissue on its dorsal aspect: a large mass, the cerebrum (the *great brain*), and a smaller, highly folded mass, the cerebellum (the *little brain*). A cerebellum with few folds or no folds at all and often of lesser relative size can be found in lampreys and all jawed vertebrates. In some fishes, the cerebellum assumes enormous proportions and, relative to the rest of the brain, dwarfs even the large cerebella of mammals and birds. What is this “little brain,” and what are its functions in various vertebrate groups? How has evolution shaped its form and connections with other brain regions? We will try to answer these questions in this chapter.

In the nineteenth and early twentieth centuries, the cerebellum was the subject of a number of functional studies that observed that surgical removal of all or part of the cerebellum resulted in disorders of movement. With the advent of progressively more sophisticated techniques for recording electrical and chemical changes in individual neurons in the middle of the twentieth century, the cerebellum became the target of intense research that unraveled the excitatory and inhibitory relationships among its neuronal constituents. Because of its consistent pattern of internal organization, its relatively few cellular components, and relatively few routes in and out, the cerebellum (in particular, the mammalian cerebellum) soon became the subject of attempts at mathematical and computer modeling of the actions of this precise neuronal network, but in spite of its deceptive appearance of simplicity, our understanding of the functions of the cerebellum is far from complete and almost certainly is strongly biased by the heavy focus

of attention on mammals as experimental subjects. Among non-mammals, the cerebellum plays an important role in the analysis of information from the lateral line system in nontetrapods as well as some amphibians. In addition, in certain groups of fishes, the cerebellum is intimately involved in the detection of electrical fields. In addition to its strong connections with the motor system, the cerebellum has major inputs from a number of sensory systems, such as the vestibular, somatosensory, visual, and auditory systems. The reader is urged to review Chapter 11, which covers the lateral line, electrosensory, and vestibular systems, before delving further into this chapter. A review of the ascending and descending pathways in the spinal cord (Chapter 8) would be useful as well.

OVERVIEW OF THE CEREBELLUM

The main divisions of the cerebellum that are common to most vertebrates are the **corpus cerebelli** (body of the cerebellum) and a **cerebellar auricle** (little ear). These are formed of an outer layer, the cerebellar cortex, and sometimes a distinct layer of white matter below. The cerebellar cortex consists of a **molecular layer** that contains relatively few cells, a **granule cell layer** that consists of small, tightly packed cells, and a layer of **Purkinje cells**, which typically have their large, pear-shaped somata located in a layer that is only one cell thick and situated between the molecular and granule cell layers. A characteristic of Purkinje cell dendrites is that they radiate in a single plane, like a tree that has been flattened into two dimensions. In jawed vertebrates other than teleosts, the Purkinje cell axon is the only pathway out of the cerebellar cortex.

In the typical vertebrate pattern, the input to the cerebellum comes from the primary or secondary nuclei of cranial nerves and from a specialized precerebellar nucleus, the **inferior olive**. Some cranial nerves, such as the vestibular and lateral line nerves, terminate directly in the cerebellum. An additional source of cerebellar afferents, particularly in mammals, is the pontine nuclei. A variety of intrinsic, inhibitory cells modulate the cerebellar input and give it its unique network properties, which will be described below. The output of the cerebellar cortex is mainly to one or more specialized **deep cerebellar nuclei** that often are located in the white matter below the cerebellum. The main targets of the cerebellar nucleus or nuclei are the **nucleus ruber** (red nucleus), which is the source of an important descending spinal pathway, and a nucleus in the dorsal thalamus for the relay of motor feedback information to the pallium. Other consistent outputs of the cerebellum are to the vestibular nuclei, the reticular formation, and the motor nuclei of the brainstem, especially those that control the movements of the eyes.

In mammals, the cerebellum is connected with the rest of the brain via three major peduncles, which are sets of efferent and/or afferent fiber tracts. The ascending projections to the red nucleus and dorsal thalamus are via the **superior cerebellar peduncle**, which is alternatively called the **brachium conjunctivum** ("conjoined arm") in reference to the interdigitation of the axons from either side of the brain as the pathways decussate at a caudal midbrain level. The superior cerebellar peduncle is not solely an efferent set of fibers; it also includes several afferent inputs to the cerebellum, including an input from the lower part of the spinal cord via the ventral spinocerebellar tract. The largest source of afferent input to the cerebellum is from the pontine nuclei, which relay neocortical inputs to it via the **middle cerebellar peduncle**, alternatively called the **brachium pontis**. Other afferent and additional efferent pathways are via the **inferior cerebellar peduncle**. This peduncle has two components—the **restiform body**, which is entirely afferent and contains the cerebellar afferents from the inferior olivary nucleus as well as the dorsal spinocerebellar and cuneocerebellar tracts, and the **juxtarestiform body**, which contains both afferent and efferent fibers that interconnect the cerebellum with the vestibular nuclei.

Descriptions of the cerebella of mammals sometimes include terms such as **paleocerebellum**, **archicerebellum**, and **neocerebellum** to refer to the relative ages or stages of evolutionary development of the major components of these structures. These terms, however, do not reflect current knowledge of the comparative anatomy and evolution of the cerebellum and its relationship with other major brain systems, such as the cerebral cortex and the corticospinal pathways. In particular, the term "neocerebellum" was applied to large lateral extensions of the cerebellum in mammals. A number of investigators of the comparative anatomy of the cerebellum now regard the avian and mammalian cerebella as having a very similar organization; therefore, if the term "neocerebellum" has any utility at all, it should be applied both to birds and mammals.

Other descriptive terms found in the cerebellum literature are **spinocerebellum**, **visuocerebellum**, **vestibulocerebellum**, and so on. These terms were introduced to draw attention to the fact that input to the cerebellum from a particular

source, such as the spinal cord, tends not to be to the entire cerebellum, but rather to specific regions. Although these terms generally are useful, they give the impression that the inputs to the cerebellum are highly segregated according to their sources. This is not entirely correct, and the reader should understand that, even though such terms are used for the convenience of discussion, considerable overlap exists between these specialized regions.

A notable exception to this general plan are teleost fishes, which have evolved certain other structures that are unique to this group of vertebrates; these include (1) a **valvula cerebelli** ("little folding doors of the cerebellum"); (2) an accessory **cerebelloid** structure, the **torus longitudinalis**, which lies at the medial edge of the optic tectum in the midbrain; (3) an additional precerebellar nucleus, the **nucleus lateralis valvulae**; (4) a **caudal lobe** located posterior to the corpus cerebelli; and (5) **eurydendroid cells** that give rise to efferent axons of the cerebellar cortex. The axons of eurydendroid cells do not terminate in specialized deep cerebellar nuclei but rather pass directly to the typical targets of the cerebellar nuclei. In fact, eurydendroid cells may be homologous as a population to the cerebellar nuclei of other vertebrate taxa.

CEREBELLAR SIZE

The size of the cerebellum varies widely across vertebrate classes. Comparisons of absolute size, however, can be misleading since many of these animals differ greatly in body size. To facilitate comparison, the brains that are shown in Figure 14-1 all have been scaled so that the hindbrain is approximately the same size in each. In addition to the cerebellum, two other major structures are shown for comparison: the mesencephalic tectum and the cerebral hemisphere. The figure shows that, in lampreys, the cerebellum is very small. It is somewhat larger in ray-finned fishes that lack electroreception and extremely large in electroreceptive fishes, such as mormyrids. As you will see later in this chapter, in those species that possess electroreception, the evolution of this sense has had dramatic effects on the size and organization of the cerebellum.

Cartilaginous fishes have cerebella that are quite substantial in size. In many species, the cerebellum has formed anterior and posterior lobes that are separated by a **primary transverse sulcus**. In some species it can be quite large with several secondary transverse sulci dividing it into folds, or **folia**.

Among the tetrapods, amphibians have relatively small cerebella. In mammals and birds, the cerebellum is quite large and very well developed. In reptiles, this structure generally has a modest size and forms a flat plate just caudal to the tectum.

No single, satisfactory explanation of this variation in relative size has been put forth. This may be due to our lack of a clear and comprehensive understanding of the functions of this major subdivision of the brain. One attractive theory had been that cerebellar size varies with the extent to which the animal moves in the vertical plane in space. Although examples exist that support this generalization, so many counter examples can be found that the theory has little predictive value.

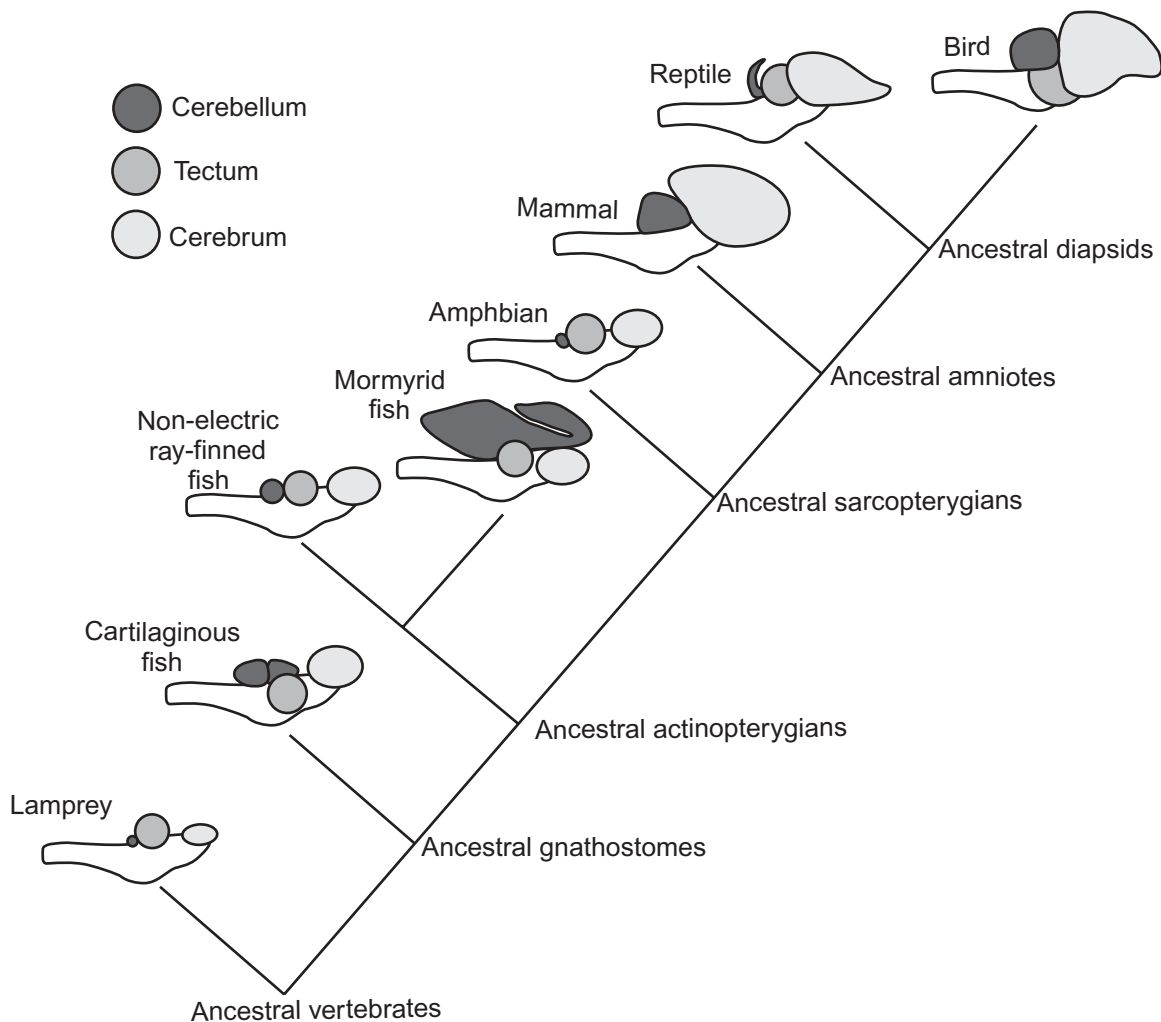


FIGURE 14-1. Cladogram to show the relative size of the cerebellum in different vertebrate classes. The species shown have widely divergent body sizes and hence different absolute brain sizes. To facilitate comparison, the hindbrains of the representatives of each class have all been scaled to the same size. Rostral is toward the right. Note the exceptionally large cerebellum of the mormyrid fish.

THE VARIOUS FORMS OF THE CEREBELLUM

Like its size, the overall form of the cerebellum, its microscopic structure, and connections to other parts of the central nervous system also vary considerably both within and between vertebrate classes. Hagfishes lack a cerebellum altogether. The cerebellum comprises only a simple ridge or plate in lampreys, some fishes, and amphibians but consists of a large, highly folded structure in some fishes and in mammals and birds. The size of the cerebellum in relation to other brain structures varies greatly in the major radiations of vertebrates.

Corpus Cerebelli

Figure 14-2 shows a classification of the more common types of configuration of the corpus cerebelli. The drawings

represent sections through the corpus cerebelli in a parasagittal plane, showing various forms of the corpus in a number of species. At the upper left is an example of one of the simpler types of cerebellar shapes, a flat plate, which is typical of amphibians and turtles. Below that are two variations in which the flat plate has been extended, which increases the area of cerebellar cortex. The plates also have been curved so that the lengthened cerebellar plate will fit within the confines of the skull. These are characteristic of alligators and lizards. In the case of lizards, however, the curvature has been in the rostral direction, which results in the granule cell layer appearing on the dorsal surface rather than the molecular layer. We have termed this a reverse curvature.

In the column of cerebellum types on the right of Figure 14-2 are other major types of variations on the flat plate cerebellum; these are various types of folding. A common form is the folded cerebellum that is characteristic of many ray-finned and fleshy-finned fishes. It consists of a single large fold, or

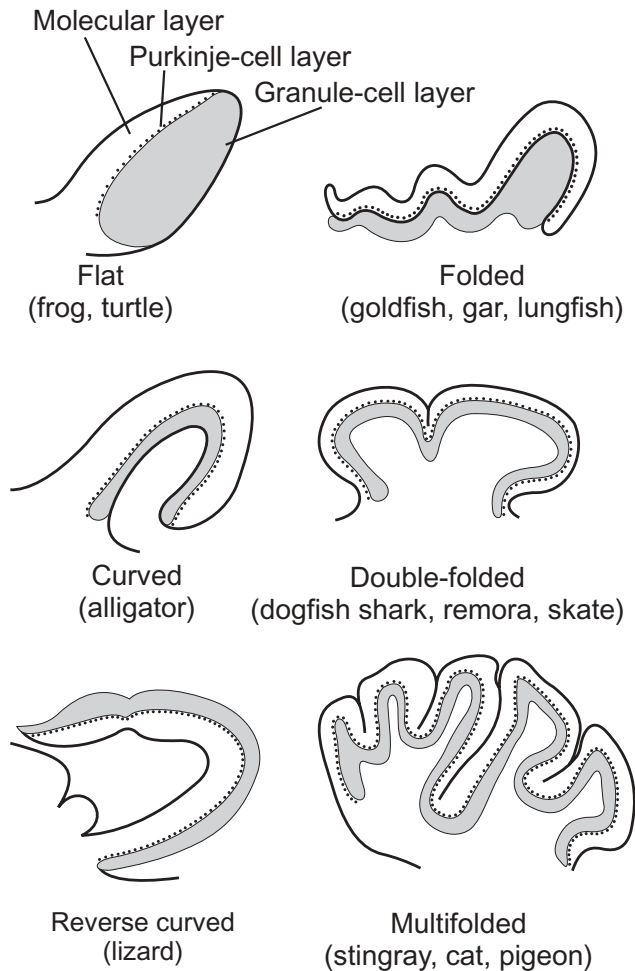


FIGURE 14-2. A classification of the form of the corpus cerebelli. Each drawing represents a parasagittal section through the corpus cerebelli. In each example, the rostral end is to the left, and the caudal end is to the right. The shaded areas represent the granule cell layers, the unshaded areas represent the molecular layers, and the dotted layers represent the Purkinje cell layers.

folium (plural = **folia**), known as the corpus cerebelli (body of the cerebellum) and a rostral extension that consists of several smaller folds, the **valvula**. A double-folded structure often is found in cartilaginous fishes. Much more elaborate folding of the cerebellum as a consequence of a massive expansion in the total surface area of the cortex can be seen in stingrays, birds, and mammals. The drawing in Figure 14-2 labeled “multifolded” shows the folding pattern of only two lobes of this type of multilobed cerebellum in which each lobe contains several folds. Birds have 10 lobules or major folia in their cerebella. Mammals also have 10 lobules in the central region known as the **vermis** (worm) and many more folds in the lateral portions of the cerebellum.

Electroreception and the Cerebellum

The most elaborate form of the cerebellum is found in the **valvula cerebelli** of mormyrid fishes. The cerebellum plays a

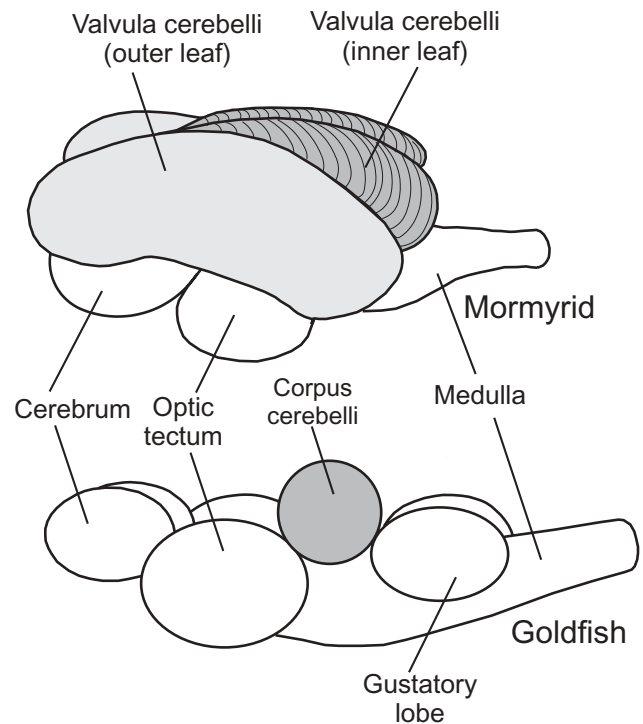


FIGURE 14-3. A comparison of the cerebella of an electroreceptive mormyrid fish (top) and a nonelectroreceptive goldfish (bottom). The portion of the mormyrid cerebellum shown is the massive **valvula cerebelli**, beneath which is hidden the **corpus cerebelli**.

major role in electroreception, and in these fishes it has evolved into a massive organ. The **valvula**, in particular, has developed into an enormous sheet of hyperfolded tissue. The mormyrid brain has carried the “packaging” technique of folding to an extreme by organizing the **valvula** into a long continuous ribbon that is folded over and over again along its length, like a wavy ribbon of toothpaste. These folds, shown in Figures 14-3 and 14-4, form thin, tight hyperfolds that provide a superb packaging arrangement for this vast sheet of cerebellar cortex. If the **valvula** of a mormyrid were to be unfolded and stretched out, it would be more than 10 times the length of the fish’s body. Indeed, the weight of the entire cerebellum can account for nearly 80% of the total weight of the brain in these animals.

A comparison of the cerebella of a mormyrid fish and a nonelectric, freshwater teleost fish, the goldfish, is shown in Figure 14-3. The goldfish cerebellum is of a size and shape that is typical of nonelectric ray-finned fishes, both teleost and non-teleost. Only the **corpus cerebelli** is visible in the intact brain; the **valvula** is tucked away within the convenient space provided by the large ventricle located in the depths of the lobe of the optic tectum.

In contrast, in the mormyrid brain shown in Figure 14-3, the **valvula** is substantially hypertrophied and has expanded beyond the confines of the tectal ventricle; thus it covers the dorsal surfaces of the **corpus cerebelli**, the **cerebrum**, and the **tectum** and overhangs the brain on the sides. Figure 14-4 shows a dorsal view of the brain of a mormyrid fish,

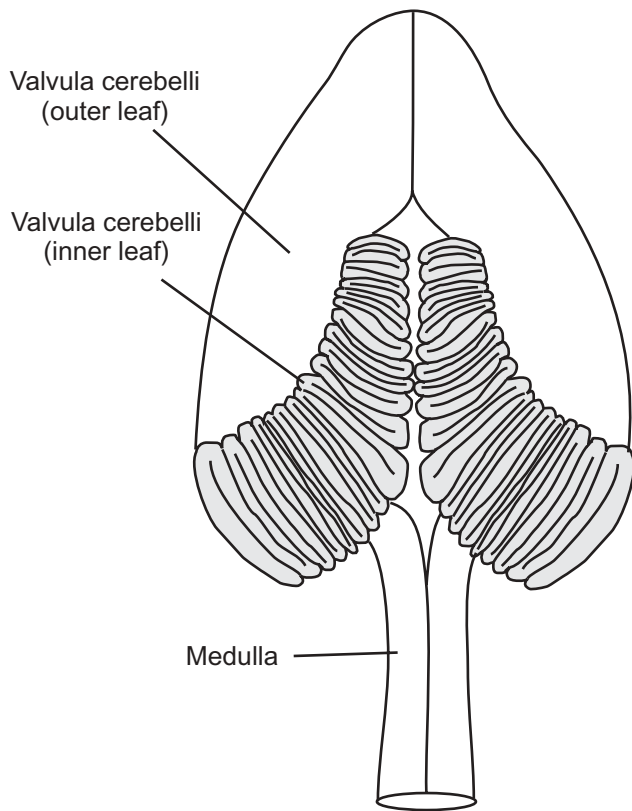


FIGURE 14-4. A dorsal view of a mormyrid brain. The valvula cerebelli completely overhangs the corpus cerebelli, the cerebral hemisphere, and the optic tectum.

in which all of the brain except the medulla has disappeared beneath the massive valvula cerebelli.

An important point is that the valvula of weakly electric fishes is highly specialized for electroreception and is a very different organ from the valvula of nonelectric fishes. The electroreception system has evolved a complex series of nuclei that have direct and indirect relations with the valvula; these are entirely lacking in nonelectric fishes. For example, in catfishes and gymnotids (which are euteloests—see Figure 4-9) and in knifefishes (notopterids) and mormyrids (which are osteoglossomorphs—see Figure 4-9), a specialized region of the octavolateralis area known as the **electrosensory lateral line lobe**, which is closely related to the cerebellum, receives the electrosensory input.

Electroreception is not confined to fishes that generate electric fields around themselves. Lampreys, cartilaginous fishes, some species of ray-finned fishes, amphibians (except frogs and toads), and the monotreme mammals possess the specialized receptors necessary to detect the very weak electric fields that normally surround an animal or that might be produced by the action potentials in the muscles of prey as they move. In fishes and amphibians, the electroreceptive lateral line system is innervated by the lateral line nerves, while in monotremes, the electroreceptors are innervated by a specialized division of the trigeminal nerve (see Chapter 11).

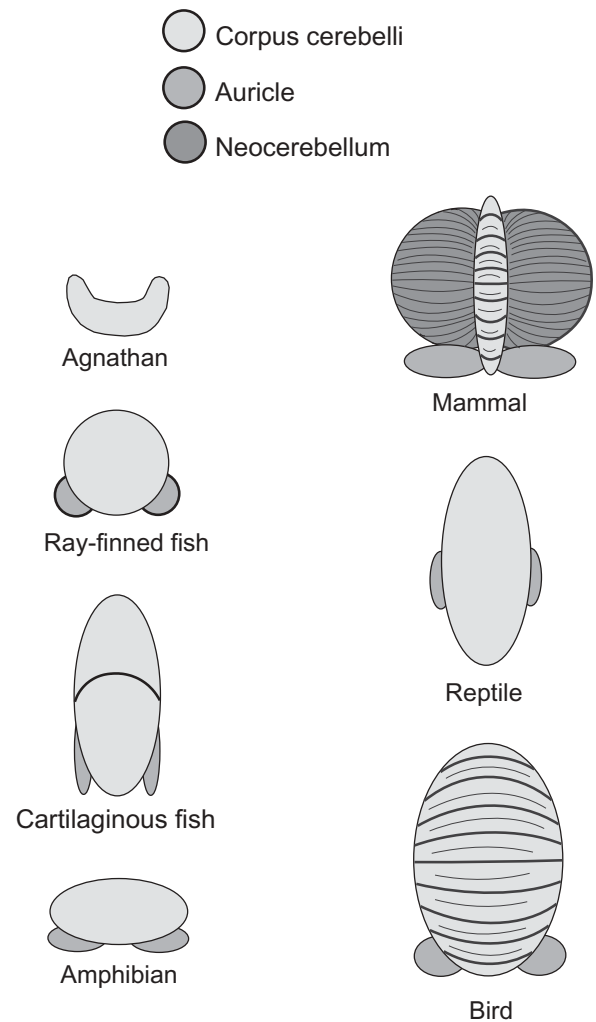


FIGURE 14-5. Schematic representations of the major components of the cerebellum in various groups of vertebrates. The valvula, a rostral extension of the corpus cerebelli unique to ray-finned fishes, has not been included here.

The Cerebellar Auricle

In addition to the corpus and the valvula, the cerebellum contains a smaller, caudal structure, usually on the ventrolateral aspect of the cerebellum. This is the cerebellar auricle. The auricle often has a multifolded conformation, and in some animals, especially sharks and rays, it is subdivided into two lobes called the **upper leaf** and the **lower leaf**. The auricle is the region of the cerebellum that receives input from the vestibular system. The output from the auricular region is especially influential on those motor neurons that control the muscles that move the eyes. In tetrapods, the auricle is known as the **flocculus**.

Phyletic Development of the Form of the Cerebellum

Figure 14-5 summarizes the main differences between the major vertebrate groups in the overall form of the cerebellum. Electrosensory ray-finned fishes, which do not fit the general

vertebrate pattern, have been omitted from the diagram. The agnathan cerebellum, present only in lampreys, is shown at the left. In lampreys, the cerebellum is rudimentary, and its correspondence to the corpus cerebelli of jawed vertebrates is unresolved. Below is the cerebellum of a nonelectrosensory ray-finned fish; note the corpus cerebelli and the auricle. In mammals, a foliated corpus cerebelli also is present as the midline **vermis**. In addition, the mammalian cerebellum shows a large, highly foliated, lateral expansion known as the neocerebellum. Similar patterns may be seen in the cerebella of cartilaginous fishes, amphibians, and reptiles. In birds, the corpus cerebelli becomes foliated into 10 folia. Whether the lateral expansion in mammals is in fact “new” or is merely a variation on the same foliated plan as seen in birds is a matter now being debated. Evidence does exist, however, to suggest that, rather than being a new addition to the cerebellum, the neocerebellum is, in fact, merely a lateral expansion of the corpus cerebelli.

THE CEREBELLA OF TETRAPODS

In general, the cerebella of tetrapods are more consistent in their cellular organization and relationships to other cell populations in the brain and spinal cord than those of nontetrapods, so we will describe those first. In tetrapods, the cerebellum comprises two principal zones: a three-layered cortex and an underlying white matter (Figure 14-6). The white matter consists of the incoming axons to the cortex and the outgoing axons from the cortex. The three layers of the cortex are a thick superficial **molecular layer**, a thin intermediate layer that typically is a sheet of large neurons only one cell thick, and a thick internal layer of very densely packed granule cells. The molecular layer consists mainly of dendrites, unmyelinated axons, and scattered cells of two distinctive types: the **stellate cells** and the **basket cells**. The intermediate layer of the cortex consists of a one-cell-thick sheet of neurons with large, pear-shaped somata and elaborate dendrites that extend into the molecular layer. These cells are the **Purkinje cells** and were first described in the nineteenth century by the Czech anatomist and physiologist Johannes Purkinje (Purkyně in Czech and pro-

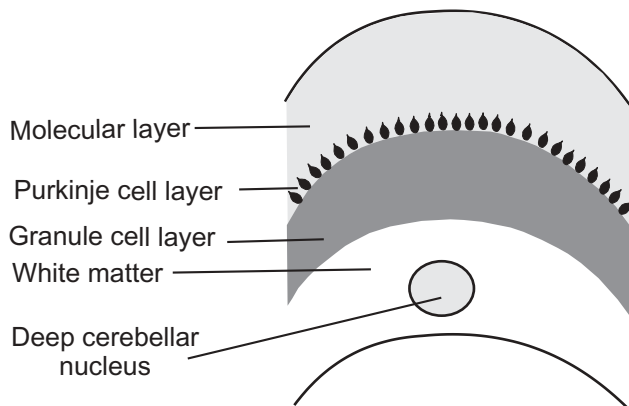


FIGURE 14-6. The lamination of the cerebellar cortex of tetrapods.

nounced “poor-kee-nyeh” although English speakers typically pronounce it “purr-kinn-jee”).

The Purkinje cells tend to be spaced more or less uniformly with some distance separating each Purkinje cell from its neighbors. The axons of the Purkinje cells, which are the only route out of the cerebellar cortex, pass through the underlying granule cell layer and enter the white matter below. Internal to the Purkinje cell layer is the layer of **granule cells**. In contrast to the Purkinje cells, granule cell somata are quite densely packed and indeed constitute the greatest density of neurons in the central nervous system. In addition to the granule cells, the granule cell layer contains three other types of cells: **Golgi cells**, **Lugaro cells**, and **unipolar brush cells** (see Box 14-1). The granule cell layer rests on the layer of white matter that contains the axons of the Purkinje cells, the axons that constitute the two main afferent pathways to the cerebellar cortex (the **mossy fibers** and the **climbing fibers**), and one or more groups of neurons that constitute the deep cerebellar nuclei. The cells of the deep cerebellar nuclei are the targets of the Purkinje cell axons. Figure 14-7 shows photomicrographs of the cerebella of a turtle and a bullfrog. In nontetrapods, a white matter layer that is clearly distinguishable from the cortex is not present; the afferent and efferent axons of the cerebellum merely mingle with those of the underlying pons.

THE CEREBELLA OF NONTETRAPODS

Agnathans and Cartilaginous Fishes

Among agnathans, the cerebellum has been identified only in lampreys, in which it consists of a simple bridge of gray matter between the right and left octavolateral areas of the rostral medulla. According to current anatomical opinion, hagfishes lack any vestige of a cerebellum. In cartilaginous fishes, the granule cells, rather than appearing in a continuous sheet to form the granule cell layer, have formed long, cylindrical columns known as the **eminentiae granulares (granular eminences)**. Two such columns lie on the roof of the ventricle that is at the core of the corpus cerebelli, and two more are situated on the floor of the cerebellar ventricle. The latter two protrude into the fourth ventricle of the medulla and pons. The eminentiae granulares are shown in Figure 14-8, which is a representation of the cerebellum and pons of the cartilaginous ratfish. The most ventral of the ventral cell columns is sometimes known as the **eminentia ventralis**. Also shown in the figure are the Purkinje cells, which congregate on the lateral walls of the corpus rather than being distributed uniformly across the cortex. The cerebellar auricles also appear in the diagram. The cerebellum in sharks (Fig. 14-9) and other cartilaginous fishes has a similar structural organization.

Ray-Finned Fishes

The cerebellar layers show considerable variation in ray-finned fishes (Fig. 14-10). In some species, the Purkinje cells are organized in a single sheet everywhere as in tetrapods. In others, the Purkinje cells are in a sheet in the corpus but are scattered in the molecular layer in the valvula. Still others have

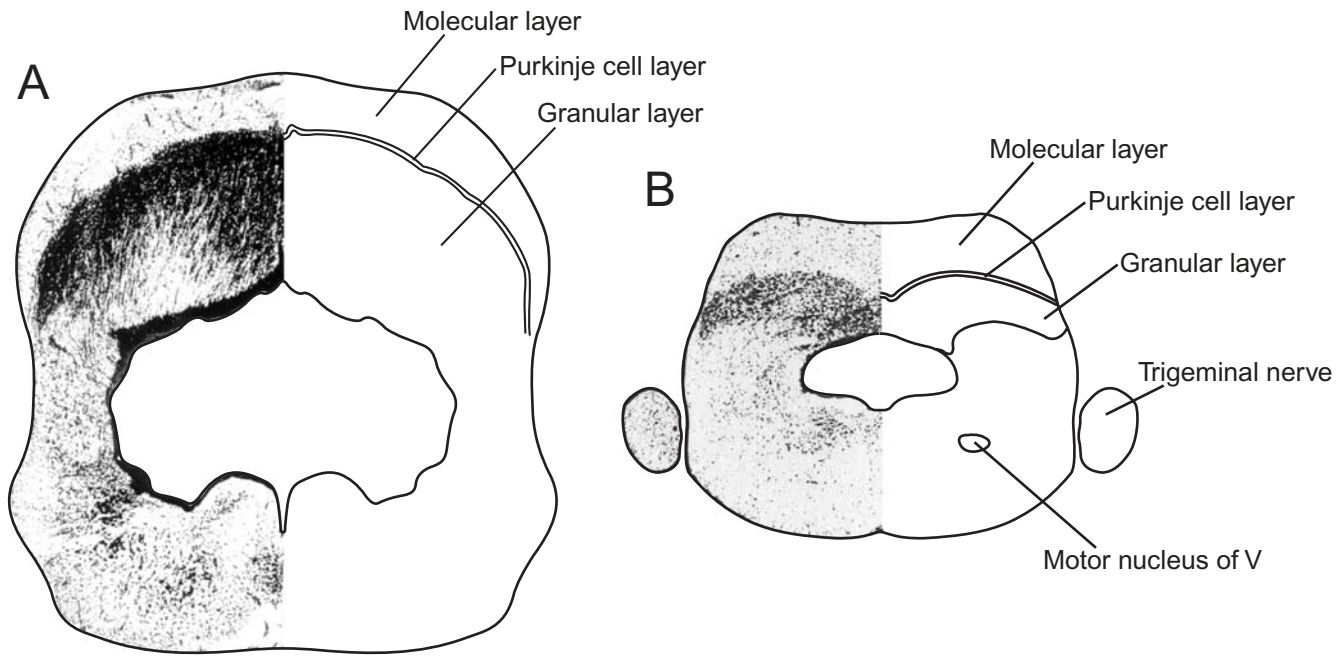


FIGURE 14-7. Transverse hemisections with mirror image drawings through the cerebellum of (A) a turtle (*Pseudemys scripta*) and (B) a bullfrog (*Rana catesbeiana*). The latter was adapted from Wilczynski and Northcutt (1983) and used with permission of John Wiley & Sons.

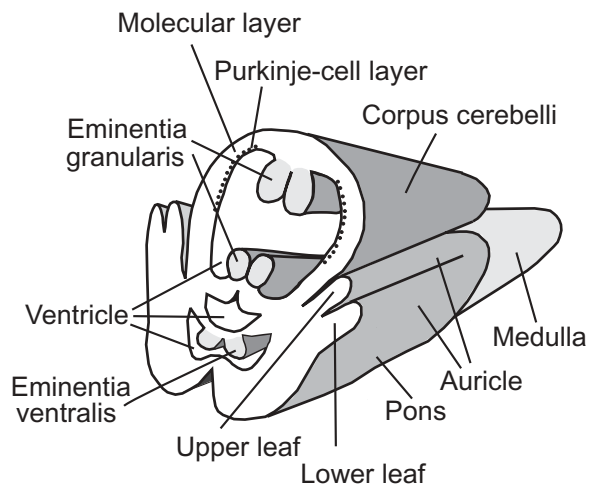


FIGURE 14-8. A drawing of the caudal half of the brain of a cartilaginous fish (a ratfish) that shows both the internal and external structure of the cerebellum.

a sheet organization in some parts of the corpus and a scattered organization elsewhere in the corpus. Some species have the granule layers located in a column lateral to the molecular layer as well as ventral to it. These lateral columns are the eminentiae granulares. An example is shown in Figure 14-11, which is a drawing of the brain of a catfish.

The principal afferents to the corpus cerebelli in ray-finned fishes are from the inferior olive, the spinal cord, the reticular formation, the torus longitudinalis, and cranial nerves

V and VIII. Among its major efferents are pathways to the red nucleus, the reticular formation, the tectum and torus semicircularis of the midbrain, cranial nerve III, the valvula cerebelli, and nucleus lateralis valvulae. The main afferents to the valvula are from the eminentia granularis, the inferior olive, and the nucleus lateralis valvulae, and various hypothalamic areas. In goldfish, the efferents of the medial lobe of valvula show a similar pattern to those from the corpus cerebelli, whereas those from the lateral lobe are to the corpus cerebelli, the vagal lobe of the medulla, and various hypothalamic areas.

THE CEREBELLAR CORTEX

The Purkinje Cell Layer

Purkinje cells are easily recognized in all jawed vertebrates. In lampreys, the cerebellum contains large, scattered neurons with widely branching dendritic trees, rather than the flattened trees of Purkinje cells as in jawed vertebrates. Moreover, these neurons are not organized into the neat, monolayer that is characteristic of the Purkinje cell layer of jawed vertebrates. Hence, these cells in lampreys often are referred to as Purkinje-like cells.

Dendrites. To understand the relationship between the dendrites of the Purkinje cells and other components of the cerebellar cortex, you must first understand the distinction between the short and long axes of a cerebellar folium. The short axis is the axis that cuts across the fold, in contrast to the long axis, which runs along the length of the fold. These axes

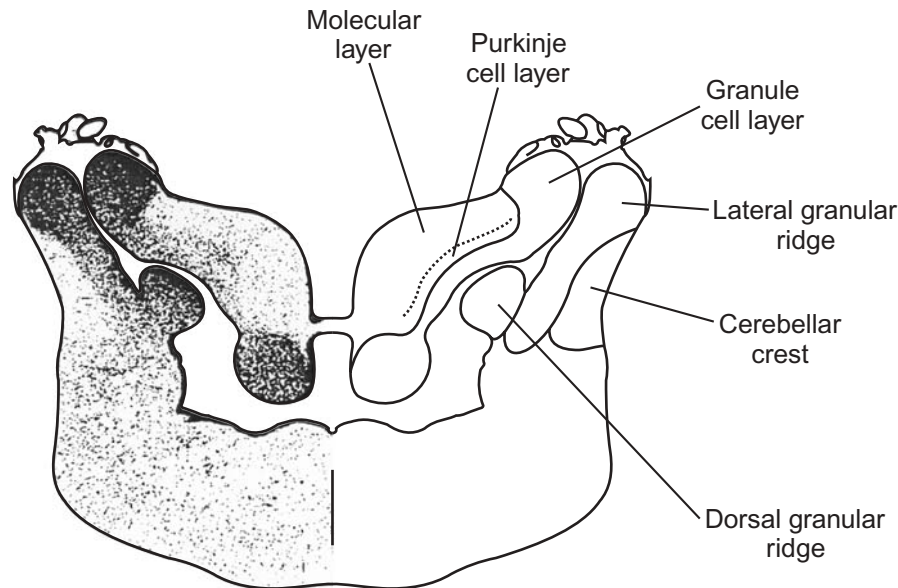


FIGURE 14-9. Transverse hemisection with mirror image drawing through the cerebellum of the horn shark (*Heterodontus francisci*). Adapted from Cruce et al. (1999) and used with permission of John Wiley & Sons.

are diagrammed in Figure 14-12. Also shown in the figure are Purkinje cells and parallel fibers, which will be described below.

The dendrites of the Purkinje cells extend up into the molecular layer and ramify (form branches) that are oriented along the short axis of the cerebellar folium. Unlike the dendritic trees of most neurons, however, which have a dendritic domain that is three dimensional, the Purkinje cell's dendritic domain is much closer to two-dimensional because virtually the entire dendritic tree is flattened along the plane of the short axis. In other words, when seen in the plane of the short axis, the Purkinje cell appears to have a rich, highly elaborate dendritic tree, but when seen in the plane of the long axis, the same cell appears to have a thin, compressed dendritic tree. Figure 14-13 shows the dendritic domains of two cells. A Golgi cell, which is one of the cell types found in the cerebellar cortex of amniotes, is shown at the top of the figure. Its dendritic domain is roughly in the form of a cube and occupies approximately the same volume in both the long and short axes of the folium. Below is the dendritic domain of a Purkinje cell, which has the form of a thin slab, with the large surface being in the plane of the short axis and the narrow surface in the plane of the long axis. The bottom shows the same dendritic domain bisected through the Purkinje cell's soma to show the appearance of its dendritic tree in the plane of the long axis. The dendritic trees of the Purkinje cells of agnathans, however, do not follow the typical pattern; they are more like that of the Golgi cell shown at the top of the figure. Figure 14-14 shows examples of the varieties of dendritic trees that can be found in Purkinje cells. These range from the relatively sparse arborizations in catfishes, to the more candelabra-like formations of rays and mormyrids, to the more tree-like arrangement in alligators and mice.

Somata. Except in agnathans in which they are scattered throughout the molecular layer, the pear-shaped somata of the

Purkinje cells are located at the border between the molecular and granule cell layers of the cerebellar cortex. They are spaced more or less uniformly apart with some separation between them. In general, at least within mammals where the most detailed studies have been done, the larger the animal (and hence the larger the brain), the larger are the Purkinje cell somata and the greater is the intercellular spacing. Although they appear morphologically identical within a single animal, individual Purkinje cells differ somewhat in size and can be classified according to the presence or absence of various neuroactive substances.

Axons. Like the giant axons of the Mauthner cells of the nontetrapod spinal cord, the initial segment of the Purkinje cell axon is thinner than the rest of the axon. These axons descend through the granule cell layer and leave the cerebellar cortex. As they do so, they give off recurrent collaterals that ascend to terminate on the somata and dendrites of Golgi cells and basket cells. The action of the Purkinje cell axon is a GABA-mediated inhibition of the cells upon which they terminate.

In all jawed vertebrates except ray-finned fishes, the Purkinje cell axons terminate in one or more specialized cerebellar nuclei and in nuclei associated with the vestibular system. A notable exception occurs in ray-finned fishes in which the Purkinje cell axons generally are not the source of the cerebellar cortical efferents, but rather remain intrinsic to the cortex, where they terminate on other Purkinje cells and on the deeper lying stellate cells. The task of carrying the results of cerebellar cortical processing to other regions of the brain falls to a group of specialized efferent cells. These cells, known as **eurydendroid** cells, also receive axon terminations of the Purkinje cells and differ from Purkinje cells in a number of ways. These differences are in the spread of the dendritic tree and the lack of spines on their dendrites. Another major difference is that the extrinsic

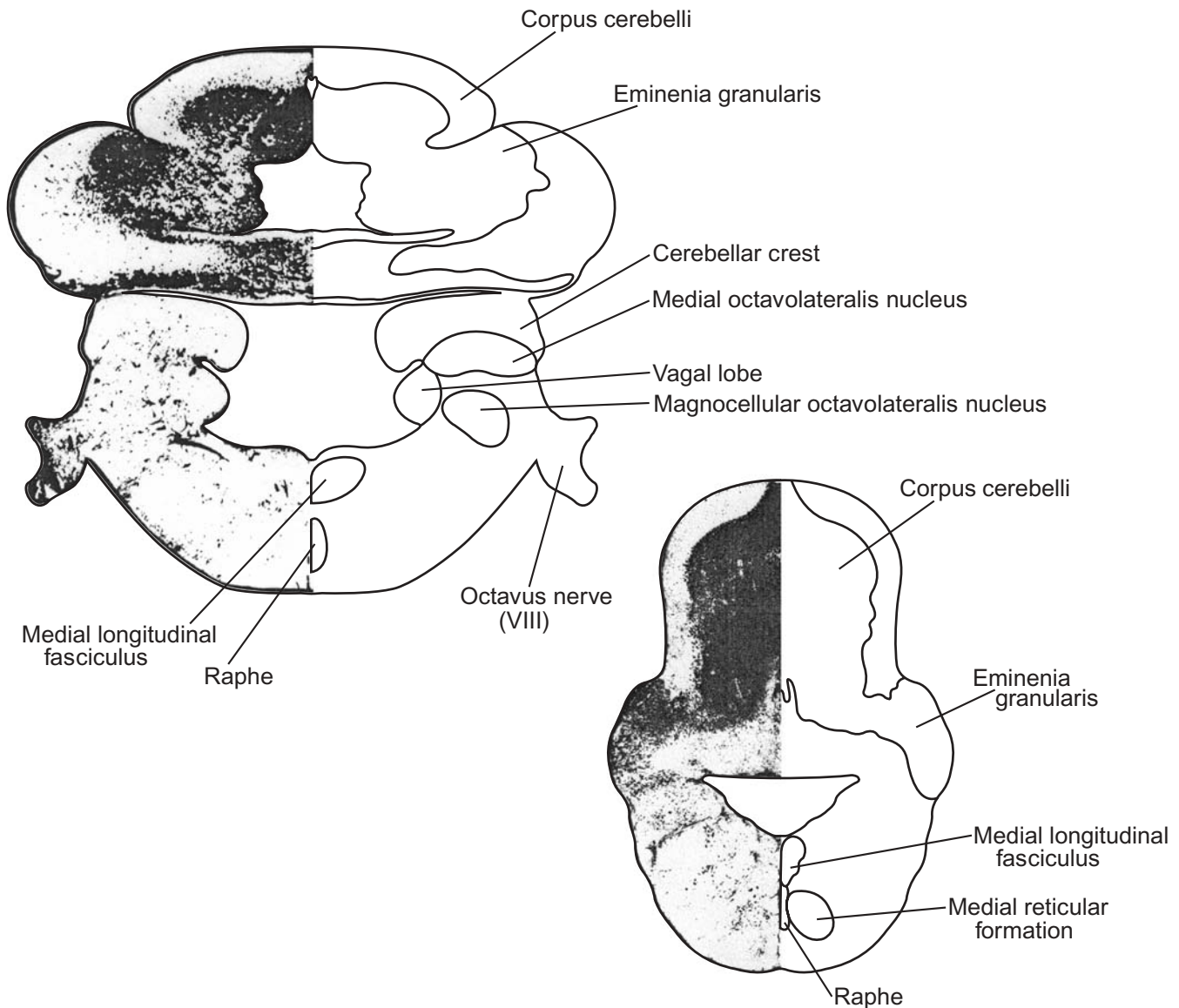


FIGURE 14-10. Transverse hemisections with mirror image drawings through the cerebellum of (left) a gar (*Lepisosteus osseus*) and (right) a teleost (*Lepomis gibbosus*). Adapted from Parent and Northcutt (1982) and Parent et al. (1978), the former used with permission of Elsevier and the latter with permission of John Wiley & Sons.

axons of the eurydendroid cells do not terminate in a deep cerebellar nucleus but rather, like the deep nuclei themselves, pass directly to target cell populations in the brainstem and spinal cord. However, not all cortical efferents are via the eurydendroid cells; a cerebello-acousticolateral pathway has been reported that originates in Purkinje cells.

The Granule Cell Layer

Granule Cell Somata. In contrast to the Purkinje cells, which are relatively large, relatively few, and can be separated by spaces at least as wide as a Purkinje cell soma or wider, the granule cells are relatively small, highly numerous, and densely packed. Indeed, the cerebellar granule cells are probably the

most densely packed cells in the central nervous system. The degree of density of the granule cells, like that of the Purkinje cells, varies with the size of the animal and the weight of the brain. Thus, smaller animals tend to have more densely packed granule cells than larger ones. For example, the number of granule cells per cubic μm of cerebellar cortex is approximately 800–1,100 in elephants and whales, 1,200–1,500 in sheep, bulls, and horses; 1,600–2,300 in humans, Old World monkeys, cats, foxes, and opossums; and 2,500–3,200 in rats, mice, and moles. Similar findings have been reported for birds in which cellular density in large birds, such as ostriches, is considerably lower than it is in small birds, such as a titmouse. With regard to the ratio of granule cells to Purkinje cells, in larger animals such as elephants, whales, porpoises, primates,

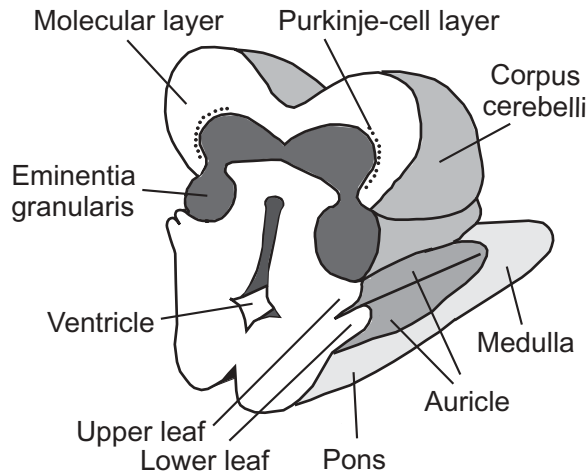


FIGURE 14-11. A drawing of the caudal half of the brain of a ray-finned fish (a catfish) that shows both the internal and external structure of the cerebellum.

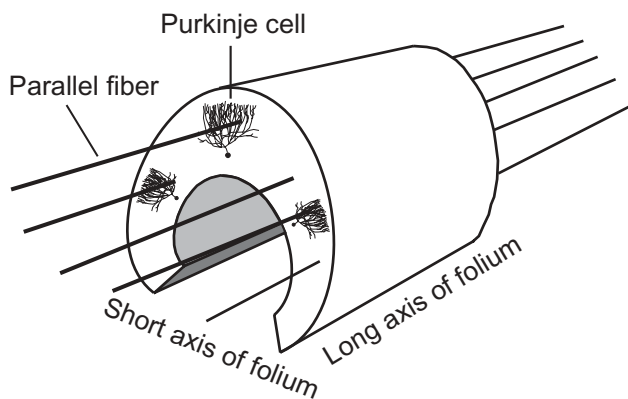


FIGURE 14-12. A schematic representation of a single folium of a cerebellar cortex. The parallel fibers run parallel to the long axis of the folium, and the Purkinje cell dendritic trees are flattened parallel to the short axis of the folium.

sheep, bulls, and horses, the ratio varies from approximately 1,500–3,000 granule cells per Purkinje cell; in the smaller animals, however, such as mice, moles, hedgehogs, rats, and guinea pigs, the ratio varies from about 600–950 granule cells per Purkinje cell. Thus, even though both Purkinje cell density and granule cell density decrease with increasing weight of the cerebellum, at least in birds and mammals, the amount of change is greater in the granule cells.

Granule Cell Dendrites. Unlike the Purkinje cells, which show a considerable degree of variation in the form of their dendritic arborization, the granule cells show a considerable degree of consistency across species as may be seen in Figure 14-15. Granule cells typically have dendrites that are relatively few (usually four or five per soma) and relatively short. The dendrites end in a characteristic claw-like formation or occasion-

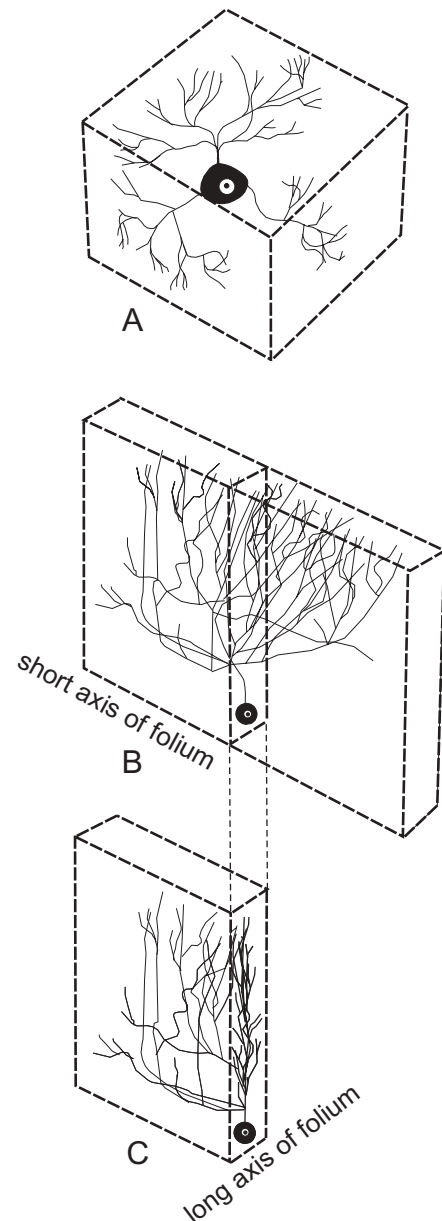


FIGURE 14-13. Dendritic domains of a Golgi and a Purkinje cell. A: The dendrites of the Golgi cell occupy a space that is roughly a cube. B: The dendritic tree of the Purkinje cell, which spreads out across the short axis of the folium, occupies a space that is roughly a solid rectangle. C: The solid rectangle of the Purkinje cell domain has been cut in the plane of the soma to reveal the appearance of the Purkinje cell as it would be seen in the plane of the long axis of the folium.

ally in a knob-like ending. These endings are the locus of termination of one of the two main types of cerebellar inputs, the mossy fibers. The mossy fiber terminations are only axodendritic; axosomatic terminations do not occur in these cells. Because of the extremely dense packing and dense staining of the granule cell somata, the regions of the granule cell layer in which the dendrites are found appear in stained tissue as little

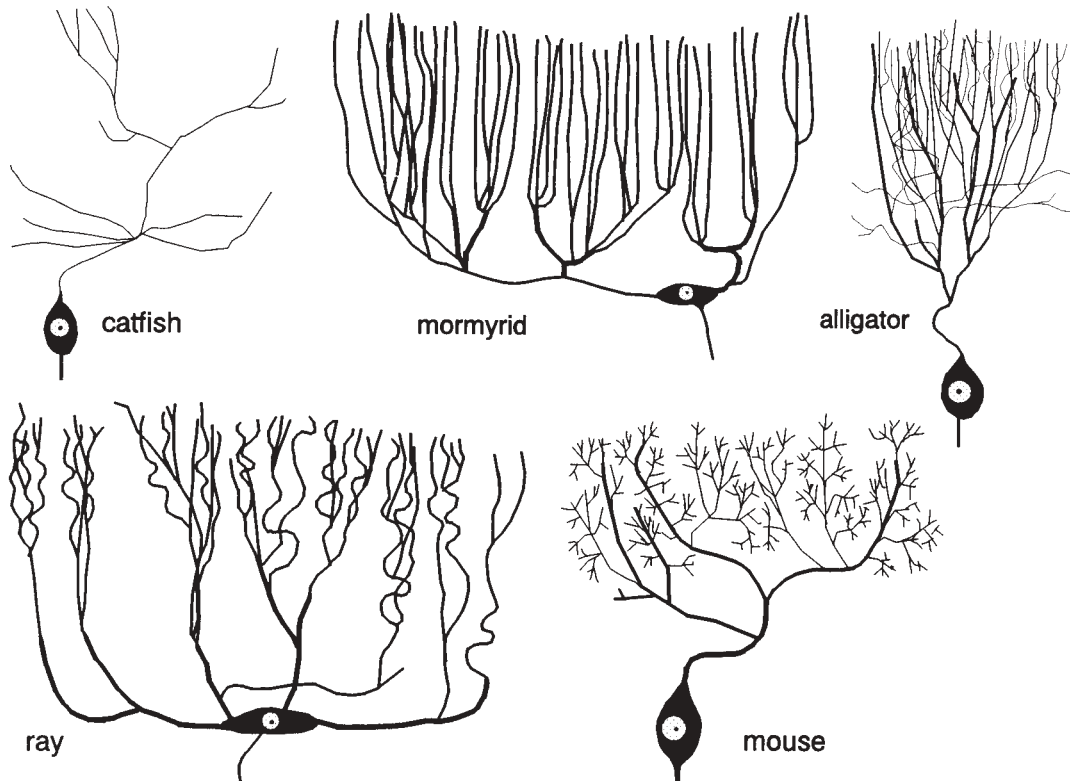


FIGURE 14-14. A sample of the differing forms of Purkinje cells among vertebrates.

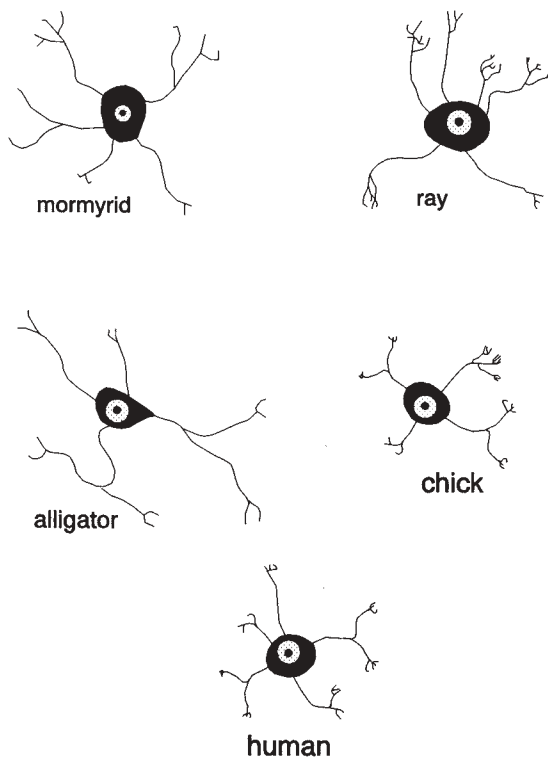


FIGURE 14-15. A sample of vertebrate granule cells. Note the similarity in dendritic organization.

islands of unstained tissue called **glomeruli**. In addition to the mossy fiber input from outside of the cerebellar cortex, an intracerebellar axon also terminates on the granule cell dendritic endings; these are the axons of the Golgi cells, which are also located in the granule cell layer. Figure 14-16 shows a granule cell with one of its dendrites receiving axonal terminations on one of its dendritic endings to form a glomerulus. The reader should note that, in this and subsequent figures that show individual granule cells, the size of the granule cell has been greatly exaggerated for the sake of visibility and understanding; the granule cells actually are much smaller in relation to the other cells of the cerebellar cortex. The figure shows an enlarged view of the glomerulus to reveal the claw-like ending of the granule cell dendrite and the terminations of the mossy fibers and Golgi cell axons.

Granule Cell Axons. The granule cell axons usually are unmyelinated. They ascend through the granule cell and Purkinje cell layers to the molecular layer where they bifurcate into branches that then travel at right angles to the main ascending axon. These branches run parallel to the long axis of the folium and are known as parallel fibers.

An illustration of a granule cell axon is shown in Figure 14-17, in which the arrows show the direction of conduction of the granule cell and Purkinje cell axons. Because the Purkinje cell dendritic tree is spread out across the plane of the short axis of the folium, the parallel fibers pass through Purkinje dendritic branches like telephone wires passing through

the branches of a tree. This may be seen in Figure 14-17, which shows a Purkinje cell as it would appear in a section parallel to the long axis of the folium. In Figure 14-18, a slab of cerebellar cortex that has been cut in the plane of the short axis is shown. This view shows the Purkinje cell dendritic tree in its wide extent. A segment of this slab has been removed to reveal

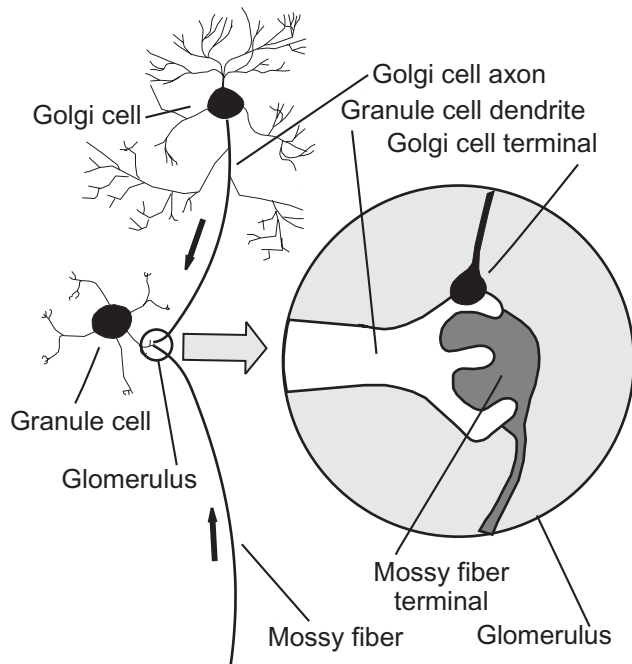


FIGURE 14-16. A cerebellar glomerulus formed by the conjunction of mossy fiber and Golgi cell terminations on the dendritic "claws" of a granule cell. The arrows show the direction of conduction of the axons. The enlarged region shows the details of one type of glomerulus.

the long-axis plane and to show the Purkinje cell dendritic tree in its narrow aspect. Several granule cells are shown in the depths of the granule cell layer. Their axons rise to the molecular layer and bifurcate to form the parallel fibers, which then

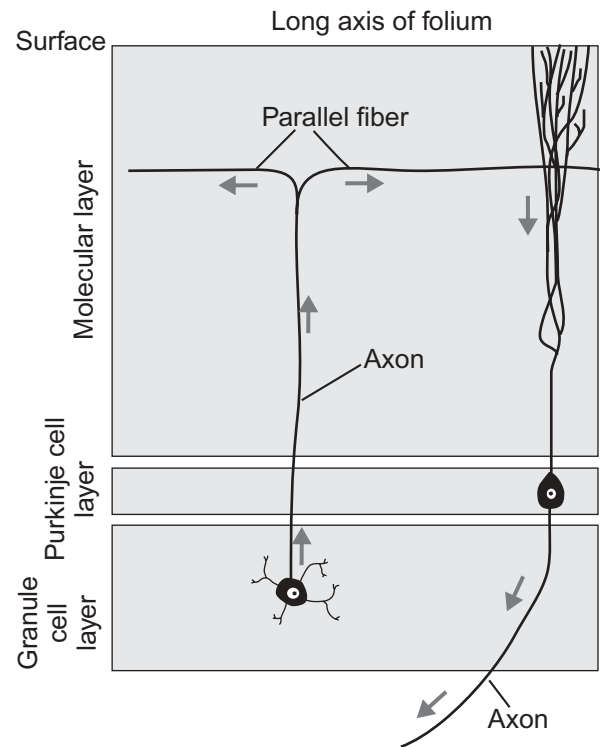


FIGURE 14-17. Granule cell axons rise into the molecular layer and bifurcate to form the parallel fibers. The parallel fibers pass through the dendritic trees of the Purkinje cells. The arrows show the direction of conduction of the axons and Purkinje cell dendrites. The size of the granule cell soma is exaggerated for better visibility.

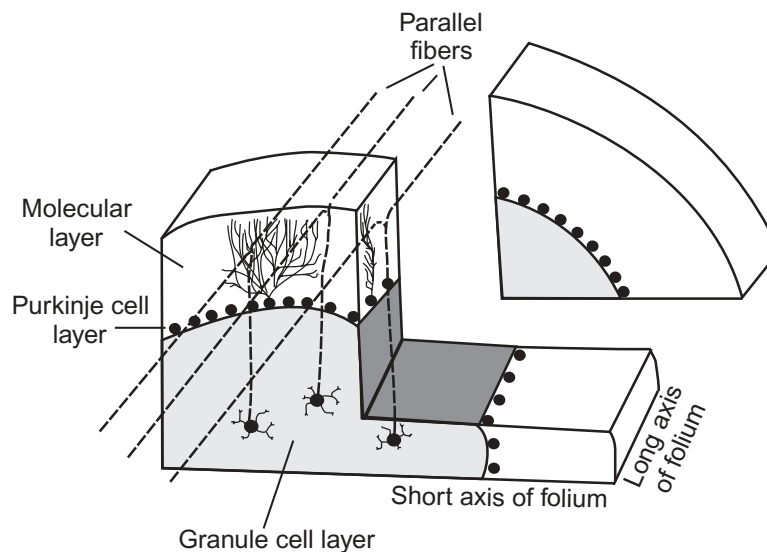


FIGURE 14-18. A schematic representation of a slab of cerebellar cortex to show the relationship between Purkinje and granule cells. A wedge of cortex has been removed to show the internal structure of the slab. The sizes of the granule cell somata are exaggerated.

run in the plane of the long axis through the branches of the Purkinje cell dendrites. The parallel fibers not only make synaptic contacts on the dendrites of the Purkinje cells, but they synapse as well on the dendrites of the other cellular constituents of the molecular layer, the basket and stellate cells. The parallel fibers of ray-finned fishes, however, do not bifurcate.

Golgi Cells. Also present in the granule cell layer are the Golgi cells, which are characterized by their large somata (a little smaller than those of the Purkinje cells), which often have numerous indentations. A Golgi cell is shown in Figure 14-19. Two types of Golgi cells have been found: those in which the dendritic tree is confined to the granule cell layer and those in which the dendritic tree extends upward into the molecular layer. The latter, which often is found in the vestibular regions of the cerebellum in birds and mammals, is receptive to input from the parallel fibers. The first type of Golgi cell mainly receives mossy fiber input on its dendrites as well as terminals from the vertical portion of the granule cell axons as they ascend to the molecular layer. The dendrites of the second type of Golgi cell additionally receive terminals from the parallel fibers. The Golgi cell axons terminate on the granule cell dendrites in the glomeruli of the granule cell layer. Golgi cells are found in cartilaginous fishes, ray-finned fishes, and tetrapods, although relatively few have been reported in amphibians.

The Molecular Layer

The molecular layer consists of the dendrites of Purkinje cells, the unmyelinated axons of the granule cells (the parallel fibers), the incoming extracerebellar afferents to the Purkinje

cell dendrites (the climbing fibers), and several cell types. The two principal cellular components of the molecular layer are the **stellate cells** and the **basket cells**, both of which are shown in Figure 14-19. The stellate cells are located in the more superficial regions of the molecular layer and the basket cells in the deeper regions. The basket cells sometimes are known as **inner-stellate** cells. The two cell types can be distinguished by their axonal terminations and their neurotransmitters.

Stellate Cells. The axons of the stellate cells extend in the long axis of the folium and run parallel to the parallel fibers. Along their course, they send out a number of collaterals that end on the dendrites of the Purkinje cells. Stellate cells have been described in sharks, teleosts, frogs, and amniotes.

Basket Cells. Like the more superficial stellate cells, the axons of the basket cells also extend in the long axis of the folium and run parallel to the parallel fibers. Their axons send collaterals with densely branched terminals to neighboring Purkinje cell somata where they form cage-like or basket-like formations (from which their name is derived) around the somata. A single mammalian basket cell typically contacts six or more nearby Purkinje cell somata. Basket cells are found most commonly in birds and mammals and less frequently in reptiles. They appear not to be present in anamniotes. Their neurotransmitter is GABA.

Afferent Inputs to the Cerebellar Cortex

Mossy Fibers. The mossy fiber input includes both primary axons of the vestibular nerve as well as secondary axons from the vestibular nuclei, spinal cord, and various cell groups

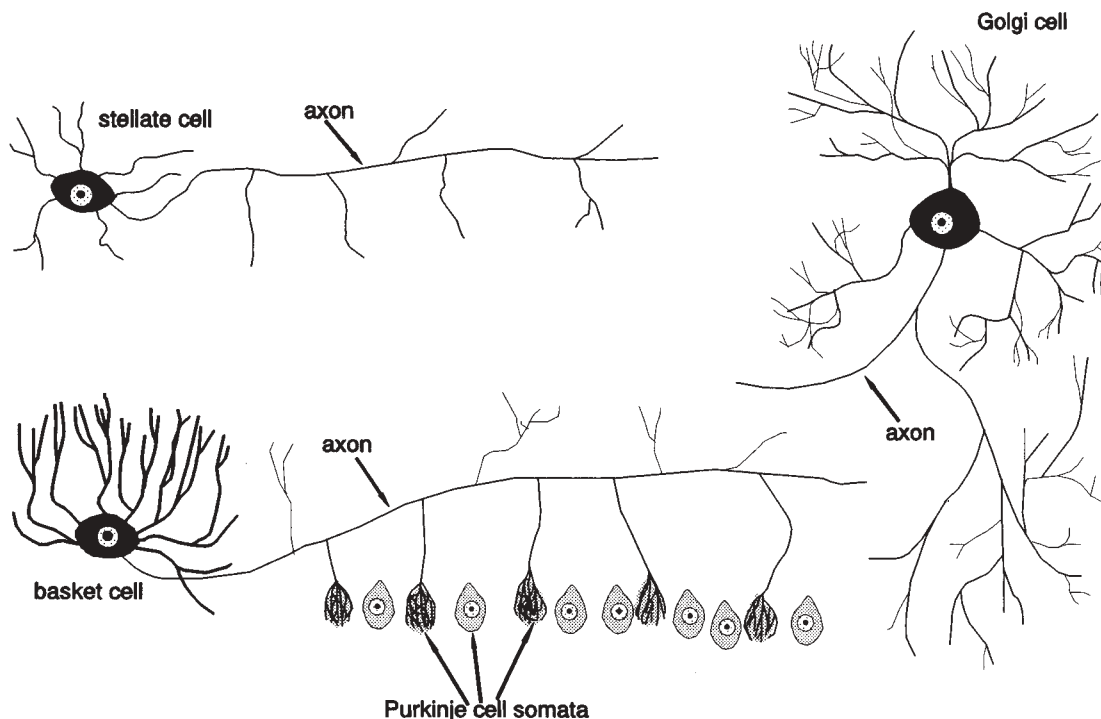


FIGURE 14-19. Illustrations of a stellate cell, a Golgi cell, and a basket cell.

BOX 14-1. Lugaro Cells and Unipolar Brush Cells

In addition to the cerebellar neuron types that are typical of all vertebrates, two additional cells types have been described in the granule cell layer—Lugaro cells and the unipolar brush cells. The Lugaro cells, first described in a mammal by Ernesto Lugaro, a 19th century Italian anatomist and psychiatrist, are bipolar fusiform cells located just below the Purkinje cell layer. Their axons ascend into the molecular layer while emitting numerous collaterals en route. They are important targets of the serotonergic input to the cerebellum from the raphe nuclei. Lugaro cells are inhibitory cells that terminate mainly on stellate cells, basket cells, and Golgi cells using GABA and glycine as their neurotransmitters. Each Lugaro cell axon terminates on 100 or more Golgi cells. They appear to provide long-range inhibition across the cortex and may function as a switching mechanism in the synchronization of cerebellar activity.

Lugaro cells have been widely reported in mammals, but so far we have encountered only one report of them in nonmammals. Two populations of Lugaro cells have been described in an *Opisthocentrus* (*Pholidapus dybowskii*), a prickly-back perciform fish of the northern Pacific. One population was revealed by the Cajal silver stain (argyrophilic type). A second population is responsive to staining for nitric oxide. The argyrophilic population is located in the corpus cerebelli, whereas the nitric oxidergic cells are mainly in the eminentia granularis. These two populations have been described as forming synaptic connections with each other and with Golgi cells and basket cells.

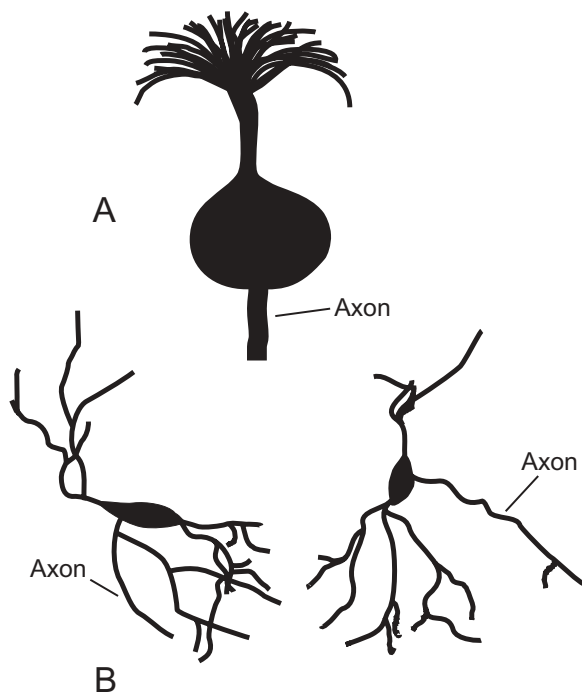


FIGURE 1. A. A mouse unipolar brush cell (adapted from Nunzi et al. (2001) and used with permission of John Wiley & Sons. B. Vertical and horizontal Lugaro cells of an *Opisthocentrus* (adapted from Pushchina and Varaksin (2001) and used with permission of Springer Science and Business Media. A and B are not drawn to the same scale.

Unipolar brush cells are characterized by their brush-like dendritic trees. They are excitatory glutamatergic neurons located in the granular layer of the vestibulocerebellum. A single incoming mossy fiber terminates on the dendritic brush to form a giant excitatory synapse. The axons of the unipolar brush cells form an intrinsic mossy fiber system that terminates in the granule cell glomeruli as well as on other unipolar brush cells. The extrinsic mossy fiber inputs to these cells arise from efferents of both the vestibular nuclei and primary vestibular nerve axons. The unipolar brush cells thus appear to contribute to vestibular excitation of the granule cells. One role that has been proposed for these cells is to provide feed-forward excitation to the granule cells that could amplify the incoming vestibular signals and also synchronize activity in functionally related granule cells. They also have been described in a cerebelloid structure, the dorsal cochlear nucleus (see Box 14-2).

Unipolar brush cells have been found in many mammalian species, including macaque monkeys, rabbits, rodents, cats, and opossums. Thus far, they have been reported only in chickens among nonmammals.

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located in the pons, including the main nuclei of the reticular formation. In mammals and to some degree in birds, the pontine nuclei are the largest source of mossy fiber input, which reaches the cerebellum via the middle cerebellar peduncle. In addition, in aquatic animals with a lateral line system, the mechanosensory lateral line nerve axons have mossy fiber terminations on the granule cells.

Each mossy fiber makes multiple terminations, each of which is on a granule cell dendrite. These terminations are known as **rosettes**. Each morphological complex formed by the claw-like or club-like endings of the granule cell dendrites, the mossy fiber rosette, and the axon terminals of the Golgi cell axons makes up a glomerulus, as shown above in Figure 14-16. The mossy fibers excite the granule cells.

Climbing Fibers. The climbing fibers are so named because they appear to intertwine themselves around the branches of the Purkinje cell dendrites much as a climbing vine wraps its tendrils around the branches and twigs of a tree. The source of the climbing fibers is much more restricted than those of the mossy fibers; it is the inferior olive, a structure located in the rostral medulla, and which will be described further below. In mammals, the inferior olivary input to the cerebellum is via the inferior cerebellar peduncle. In teleost and cartilaginous fishes, the climbing fibers do not ascend throughout the molecular layer; instead, they terminate on that part of the dendritic tree that is closest to the soma.

Additional Inputs to the Cerebellar Cortex. In addition to the mossy and climbing fiber afferent pathways, other inputs to the cerebellar cortex are more diffuse and categorized as multilayered. One that is inhibitory has been described from the **locus coeruleus** (see Chapter 13). Unlike the mossy and climbing fiber inputs, which have very specific targets, the locus coeruleus input is widespread throughout the cortex, and its terminations occur on a variety of cortical components. The inhibition results from the action of norepinephrine, which ultimately results in a hyperpolarization (inhibition) of the Purkinje cell. The locus coeruleus inputs reach the cerebellum via the superior cerebellar peduncle. Inputs from the hypothalamus and raphe nuclei also reach the cerebellum via this route.

Interconnections Within the Cerebellar Cortex

The limited afferent and efferent pathways of the cerebellar cortex have held a particular fascination for neurophysiologists and those who do research on mathematical and/or computer models of neural networks. The two main routes into the cerebellar cortex are the mossy fibers, which terminate on the granule cells and the climbing fibers, which end on the Purkinje cell dendrites. The only route out of the cerebellar cortex is the axon of the Purkinje cell or, in ray-finned fishes, the eurydendroid cells (probably homologous to cerebellar nuclei).

The basic circuitry of the cerebellar cortex, which is common to most jawed vertebrates, consists of:

- The mossy fiber → granule cell → parallel fiber → Purkinje cell excitatory input pathway

- The climbing fiber → Purkinje cell excitatory input pathway
- The Purkinje cell axon inhibitory output pathway
- The stellate cell → Purkinje cell dendrite inhibitory pathway

As the cerebellum has evolved to satisfy the adaptive requirements of various species, these pathways have been augmented by a variety of additional pathways, among which are

- The basket cell → Purkinje cell soma and dendrite inhibitory pathway
- The Golgi cell → granule cell inhibitory pathway

Regional Variations in the Cerebellar Cortex. Although the cerebellar cortex generally appears to be uniform from region to region, a regional organization can be recognized on the basis of its connections with other parts of the nervous system, the relative density of cellular components, and the presence of certain neuroactive chemical substances in specific regions. For example, in cartilaginous and ray-finned fishes, the corpus cerebelli mainly receives input from the spinal cord, while the valvula receives fibers from the lateral line system and the auricles from the vestibular system. Within the corpus, a topological representation of the body has been found in which the spinocerebellar axons from the caudal parts of the spinal cord terminate in the caudal levels of the corpus and those from the rostral levels of the cord terminate more rostrally in the corpus. The head of the animal is represented in the most rostral end of the corpus. This general pattern of topographic organization also occurs in the cerebella of tetrapods. Finally, the density of various cell types that make up the cerebellum also varies in different regions of the cerebellum.

Compartmentalization. With regard to locations of various neuroactive substances in the cerebellum, a rather dramatic parcellation or compartmentalization has been observed in a variety of vertebrates. Thus, acetylcholinesterase (AChE), an enzyme associated with the neurotransmitter acetylcholine, is present in the outer (molecular) layer of the cerebellum in distinct bands that are uniformly distributed. Likewise, another neuroactive enzyme, glutamic acid decarboxylase (GAD) and the peptide motilin also have been found located in bands or microcompartments that are separated by other bands or compartments that are free of these substances. Various other substances also have been found to exist in bands or compartments. For example, when the cerebellum is selectively stained to detect the presence of a class of peptides known as **zebrins**, the cerebellar cortex takes the stripped appearance of a zebra. The zebrin immunoreactivity appears to be specific to Purkinje cells. Some zebrin bands include regions of the cerebellar cortex that have been identified with several types of motor learning, such as eye-blink conditioning.

Zebrin II bands have been reported in the cerebella of various teleost fishes, stingrays, chicken, various rodents and primates, and opossums. In teleosts and stingrays, the zebrin immunoreactivity occurs in all Purkinje cells, and no pattern of banding is seen. Zebrin II immunoreactivity appears to be

entirely lacking anywhere in the brains of adult lampreys, although it does appear in the anterior octavomotor nucleus in juveniles. This observation offers some support for the view that the Purkinje-like cells of lampreys may not be true Purkinje cells.

Circuitry of the Cerebellar Cortex. A detailed description of the physiology of the cerebellar cortex is beyond the scope of this introductory anatomical description. In brief, however, the climbing fibers excite the Purkinje cells directly. The mossy fibers excite the granule cells, which in turn excite the Purkinje cells via the parallel fibers. The parallel fibers also excite whichever inhibitory cells are present; these in turn inhibit the Purkinje and granule cells. An example from mammalian cerebellar cortex is shown in Figure 14-20. In this figure, the Purkinje cell is represented schematically with candelabra-like dendrites. A climbing fiber is seen wrapped around one branch of the Purkinje cell dendritic tree; its terminals are excitatory. Beside the climbing fiber is a mossy fiber that terminates in an excitatory ending on a granule cell dendrite. The granule cell axon rises to the molecular layer and gives off an excitatory terminal on a Purkinje dendrite after which it bifurcates and forms the parallel fibers. The parallel fibers have excitatory terminations on the dendrites of the basket, the stellate, and the Golgi cell. The two molecular layer inhibitory cells send their axons to the Purkinje cell (the stellate cell to the Purkinje cell dendrites and the basket cell to the Purkinje cell soma) where they terminate in inhibitory endings. Similarly, the granule cell layer inhibitory cell, the Golgi cell, sends its axon to the granule cell dendrite.

Although the spread of the parallel fibers along the long axis of the cerebellar folium can be considerable (several millimeters in a large cerebellum) with synaptic endings on a large number of Purkinje cell dendrites, nevertheless a special relationship exists between a Purkinje cell and those granule cells that are directly below it. This results because the vertical portion of the granule cell axon makes synaptic contact with the Purkinje cell dendritic tree close to the soma (Fig. 14-20), which makes its excitatory action much more effective than would be the same stimulation farther out on the dendritic tree. The vertical portion of the granule cell axon, therefore, is much more decisive in affecting the probability of an action potential being generated in a Purkinje cell axon than is the horizontal (parallel fiber) portion of the same axon. A Purkinje cell and those granule cells that are directly below it in the upper levels of the granule cell layer (which have a better chance of contacting Purkinje cell dendrites before their axons bifurcate into parallel fibers) constitute a kind of functional unit. Thus, the vertical portion of the granule cell axon seems to have the main responsibility for Purkinje cell activation, whereas the parallel fibers seem to be more involved with the modulation of that excitation. One could say that the vertical granule cell axon excites the Purkinje cell, and the horizontal (parallel fiber) portion spreads the news of this excitation to other Purkinje cells and to those inhibitory cells that will modulate that excitation or suppress it entirely. This dual role of the granule cell axon is an excellent example of how cellular architecture can be as effective in determining one neuron's influence on other neurons as are the types of neuroactive substances in its axon terminals. One should note that the

region of termination of the upper granule cells on the lower region of the Purkinje cell dendrite is the same region on which the climbing fibers terminate in ray-finned fishes.

The Precerebellar Nuclei

Several neuronal populations send all or nearly all of their efferent axons to the cerebellum. These are collectively known as the precerebellar nuclei. Among these are the cell populations of the spinal cord that give rise to the spinocerebellar tracts, the funicular nuclei, the nucleus solitarius, the principal nucleus of the trigeminal nerve, the locus coeruleus, the inferior olive, and the pontine nuclei. In ray-finned fishes, an additional precerebellar nucleus is found; this is the **nucleus lateralis valvulae (lateral nucleus of the valvula)**.

Inferior Olive. The inferior olive, which is located in the rostral medulla and is the source of the climbing fibers, is an unusual neuronal population because its neurons are capable of prolonged oscillatory activity. The inferior olive appears to be present in all vertebrate classes and is particularly well developed in species with a well-developed cerebellum. In birds and mammals, the inferior olive is subdivided into a **main inferior olivary nucleus** and one or more **accessory olivary nuclei**, which are together known as the **inferior olivary complex**. The inferior olivary complex receives afferents from very diverse sources, among which are the spinal cord, reticular formation, tectum, red nucleus, neocortex, and various cranial nerve nuclei.

Nucleus Lateralis Valvulae. Unlike the inferior olive, which is located in the rostral medulla, the nucleus lateralis valvulae of ray-finned fishes is found in the tegmentum of the midbrain. Like the inferior olive, however, it receives axons from a number of neuronal populations and in turn supplies mossy fibers to the granule cells, in this case in both the corpus cerebelli and the valvula. The neurons of the nucleus lateralis valvulae are unusual in that they have no dendrites. Their main efferent target is the corpus cerebelli. The nucleus is especially large in fishes with a gigantocerebellum where it can have many subdivisions.

Pontine Nuclei. The pontine nuclei are the major source of mossy fiber input to the cerebellar cortex in birds and mammals. In birds, the pontine nuclei consist of two small cell groups in the rostral medulla that receive their input mainly from the striatum of the telencephalon, the tectum, and the spinal cord. In mammals, the pontine relay is much more substantial than in any other vertebrate group. Six main pontine nuclear groups are recognized. They receive their afferents from the tectum, the spinal cord, and the neocortex of the telencephalon. Pontine nuclei have not been identified with any certainty in reptiles and may thus have evolved separately in birds and mammals.

Nucleus Paracommissuralis. An additional precerebellar nucleus has been reported in a number of ray-finned teleost fishes—the **nucleus paracommissuralis**, which is located dorsal to the posterior commissure at the junction of the midbrain and the pretectum. This nucleus receives input from the

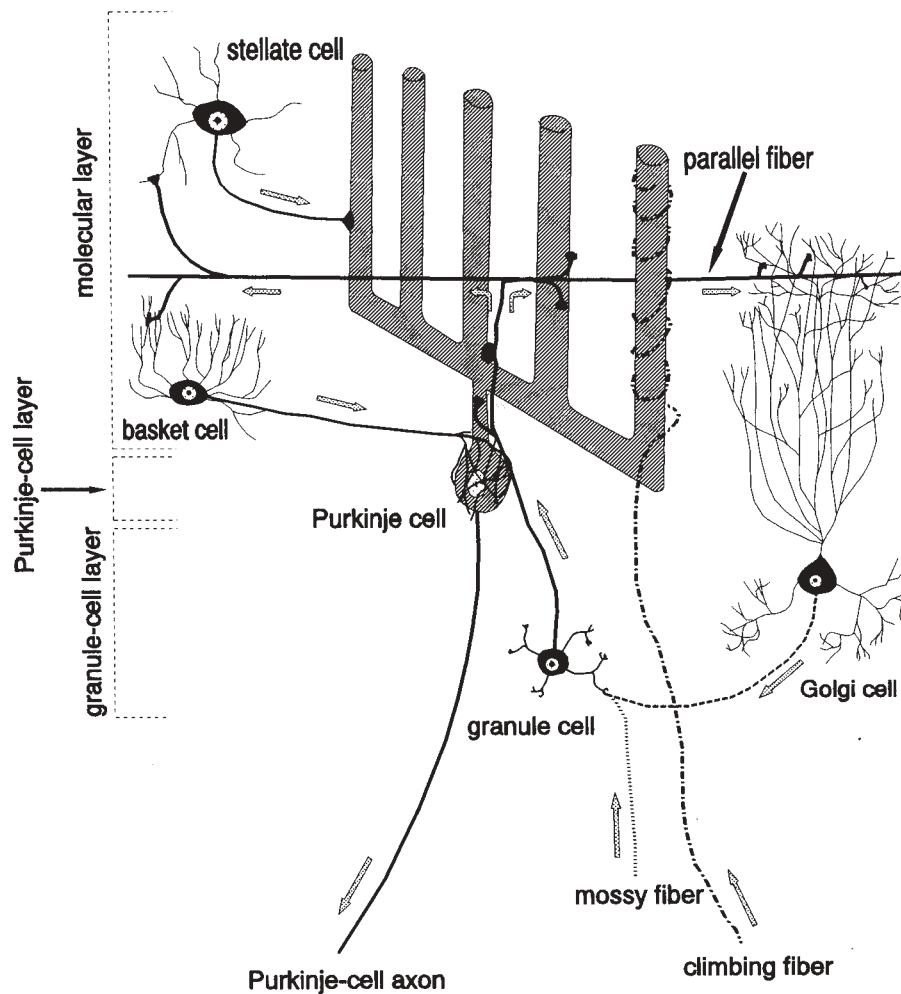


FIGURE 14-20. A schematic representation of the major cellular components of the cerebellar cortex and their interrelations. The arrows indicate the direction of axonal conduction. Mossy fibers and climbing fibers excite the granule cell and the Purkinje cell. The granule cell axon excites the Purkinje cell as it ascends through the molecular layer. The granule cell axon then bifurcates to form parallel fibers that further excite the Purkinje dendrites as well as the Golgi cell, stellate cell, and basket cell. The axon terminals of the latter three cell types are inhibitory, and thus the stellate cell inhibits the Purkinje cell on its dendritic tree, the basket cell inhibits the Purkinje cell on its soma, and the Golgi cell inhibits the granule cell. Arrows show the direction of axonal conduction.

telencephalon and sends its axons to the cerebellum. It also projects to the torus longitudinalis.

Cerebelloid Structures Associated With the Cerebellum in Nontetrapods

In addition to the valvula, the cerebella of nontetrapods have several other structures that have a cerebellum-like (cerebelloid) organization; these are the **crista cerebellaris** (cerebellar crest), the **torus longitudinalis**, and the **electroreceptive lateral line lobe** of electrosensory fishes. Some authorities have argued that, despite their spatial separation from the main structures of the cerebellum, these cerebelloid structures should be considered as part of the cerebellum rather than as separate entities.

The Crista Cerebellaris. The crista cerebellaris has an appearance similar to that of the molecular layer of the corpus cerebelli, with which it is continuous. It is found just dorsal to the lateral line sensory areas in the rostral medulla and caudal pons. It consists of a layer of parallel fibers that have their granule cell somata in the eminentiae granulares. Nearby to the crista are Purkinje-like cells, which send their dendrites into it. The crista is present in lampreys, sharks, lungfishes, *Latimeria*, holosteans (gars and bowfins—see Figure 4-6), and teleosts.

The Torus Longitudinalis. The torus longitudinalis is a common feature on the roof of the tectal ventricle in teleost fishes. It is situated close to the midline of the midbrain, just

dorsal (and sometimes rostral) to the valvula. It consists of a column of granule cells and receives some of its afferents from a cell group called the **nucleus subvalvularis**, which lies ventral to the nucleus lateralis valvulae. Other sources of afferents to the torus longitudinalis are another hindbrain cell group, the nucleus subeminentialis pars magnocellularis, some neurons that lie along a neighboring fiber tract, cell groups within the pretectum, and the midbrain roof. The torus longitudinalis contains a population of neurons that projects to the stratum marginale, or marginal layer, of the optic tectum (see also Chapter 18), as well as to the pretectum and the corpus cerebelli. The torus longitudinalis appears to relay descending forebrain inputs related to the visuomotor system to the corpus cerebelli.

One possible function for the torus longitudinalis is a role in the **dorsal light reflex**. When most fishes are situated vertically in the water, the dorsal surface of the body is oriented toward the water's surface, which is the normal source of any illumination that is present. If an experimenter provides a light source that comes from some direction other than above the fish, the animal tries to orient itself with its dorsal surface toward the light. This response is known as the dorsal light reflex. One explanation of this reflex is that the animal is responding to an imbalance in the illumination of the ventral retinas of its two eyes. Lesions of the torus longitudinalis result in a significant reduction in the dorsal light reflex, which is consistent with its hypothesized role in visual input to the corpus cerebelli.

BOX 14-2. Is There More Than One Cerebellum in the Brain?

Among the characteristics that define the cerebellar cortex are Purkinje or Purkinje-like cells that send their dendrites into the molecular layer, granule cells that send their axons into the molecular layer where they form parallel fibers that contact the dendrites of the Purkinje or Purkinje-like cells, a variety of inhibitory cells, and a sensory input that is organized topographically. We have already seen that this structural organization can also be found in a several cerebelloid structures associated with the cerebella of fishes, such as the crista cerebellaris and the torus longitudinalis. One could argue that the similarity of cell types and organization indicates that these structures should be considered as part of the cerebellum rather than separate entities. Perhaps they should, but a cerebelloid organization is also found in brain regions that are quite distinct from the cerebellum, such as the electrosensory lateral line lobe and/or the octavolateralis nuclei of teleost fishes and the dorsal cochlear nuclei of mammals.

Enrico Mugnaini and his colleagues report that the dorsal cochlear nucleus, which receives incoming axons from the cochlear division of cranial nerve VIII, has a cerebelloid type of organization that includes granule cells that form parallel fibers and efferent neurons that send their dendrites into the layer of parallel fibers. In addition, it contains inhibitory neurons, unipolar brush cells, and a topographic organization of its sensory input. Moreover, Debora Wright and David Ryugo have described a mossy fiber input to the dorsal cochlear nucleus from the nucleus cuneatus of the caudal medulla, which receives ascending somatosensory information from the upper thoracic and cervical spinal cord. One interpretation of the functional role of the dorsal cochlear nucleus is that it may serve as a kind of acoustical cerebellum that is specialized for the stabilization of head and pinna movements in relation to an unexpected sound source.

Curtis Bell and his colleagues have offered an attractive hypothesis for a common function of all cerebelloid struc-

tures, including the cerebellum itself, i.e., that they suppress predictable sensory events so that unpredictable events may be more easily detected. Accurate detection of unpredictable events, such as sudden indication of the presence of a predator or prey, an unexpected sound, or unanticipated changes in body position or locomotor pattern, can be much more important to survival than the detection of highly predictable or periodic events that can be detected by intermittent sampling.

What might be the mechanism for the appearance of these similar cerebelloid structures in the octavolateralis/cerebellum region in phylogenetically diverse taxa? One possibility might be that they result in the phenotype from the expression of a common, genetically driven, developmental program. Such structures could then be favored by selection pressures.

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THE EXCEPTIONAL CEREBELLA OF WEAKLY ELECTRIC FISHES

A number of aquatic animals are capable of generating electric currents from a specialized electric organ (see Chapter 12). The best known of these are the electric eel (*Electrophorus electricus*) and the electric catfish (*Malapterurus electricus*) among the teleosts and the torpedo or electric ray (*Torpedo nobiliana*) among the cartilaginous fishes. These animals are capable of generating quite powerful currents that can stun or kill another animal. Less well known are two orders of fresh water teleosts, the Mormyriiformes and the Gymnotiiformes, that generate electric fields of much weaker intensity than those of the electric eel or the torpedo and hence are known as the weakly electric fishes. Although many similarities exist between the electroreception systems and cerebella of these two orders, they appear to have evolved electroreception independently of each other.

The cerebella of the weakly electric fishes is the most elaborate and sophisticated of any of the fishes; some might argue that they are among the most specialized structures in any central nervous system. Like other fishes, the cerebellum in these two orders consists of a corpus cerebelli and a valvula. The cerebellum in gymnotids is smaller and less developed than in mormyrids. In addition, the gymnotid valvula does not show the highly sophisticated structure of the mormyrids. The corpus cerebelli of mormyrids comprises four lobes that have been designated C1, C2, C3, and C4. The valvula is enormous and consists of a hyperfolded sheet that contains the same organization of a granule cell layer, a molecular layer, and a Purkinje cell layer as the corpus cerebelli. Between these two structures is a smaller entity, the **lobus transitorius**. Here, however, the similarities to conventional cerebellar organization end. To begin with, although these animals have a precerebellar projection from the inferior olive, the axons of this projection do not climb into the molecular layer. Moreover, the axons of the granule cells do not make the characteristic T-shaped bifurcation within the molecular layer as they form the parallel fibers.

The interrelations between the electrosensory system and the cerebellum in weakly electric fishes have been the subject of intensive research that has revealed a complex organization of nuclear groups that have rich interconnections. The massive input from electroreceptors and other sensory systems, as well as other evidence, has led some workers to suggest that the mormyrid cerebellum may have relatively little to do with motor functions but rather has evolved into a highly sophisticated sensory processing system that permits the animal to exploit its murky environment. The weak electric fields that are generated by mormyrids are used for social recognition, mate selection, and communication, as well as the exploration of the environment by a type of electrosensory scene analysis.

The **electrosensory lateral line lobe** of mormyrids receives the axons of the three types of electrosensory receptors in the animal's skin—**mormyromasts** and **knollenorgan receptors** (both of which are subtypes of tuberous receptors) and **ampullae**. The mormyromast and ampullary receptors terminate in the electrosensory lateral line lobe, which has a

structure similar to that of the cerebellar cortex. The knollenorgan pathway ends in the nucleus of the electrosensory lateral line lobe.

In mormyrids, the electrosensory lateral line lobe consists of a molecular layer and a series of thinner layers: a ganglion cell layer, a plexiform layer, a granule cell layer, an intermediate cell and fiber layer, and a deep fiber layer. The medium cells of the ganglion cell layer have been described as Purkinje-like. Longitudinally, the lobe has three zones, a medial zone, a dorsolateral zone, and a ventrolateral zone. Each zone contains a separate map based on one of the three types of electroreceptors on the fish's body surface. The electrosensory lateral line lobe of gymnotids, which have evolved this system independently of the mormyrids, has a similar but not identical pattern of layers and organization. Their electrosensory lateral line lobes differ in their physiology as well. Among the proposed functions of the electrosensory lateral line lobe in both mormyrids and gymnotids are the suppression of electrosensory noise resulting from the electric organ discharge, as well as the suppression of other predictable stimuli, in order to maximize the detection of unpredictable stimuli of biological relevance.

The nucleus of the electrosensory lateral line lobe, which receives input from the knollenorgan receptors, is located in the deep part of the lateral line lobe. Its efferents, after synapsing in several intermediate nuclei, eventually end in the valvula. The efferents of the electrosensory lateral line lobe itself terminate in the lateral toral nucleus, which in turn sends its axons to the valvula.

Another nucleus closely associated with the electrosensory lateral line lobe is the **nucleus preeminentialis** or **preeminential nucleus** (see Figure 14-21). This nucleus, which is

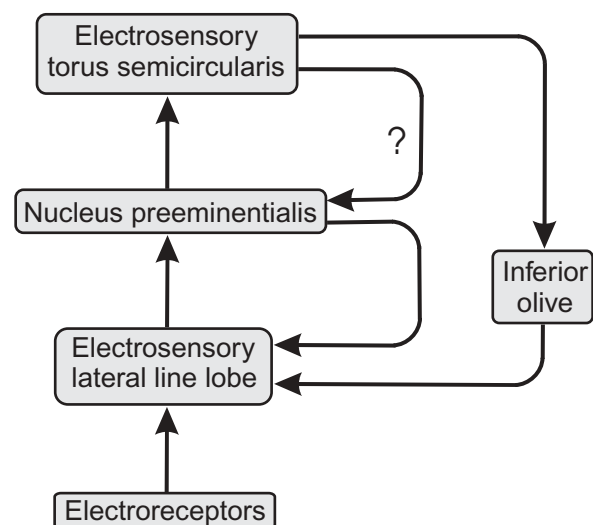


FIGURE 14-21. Feedback control of the electrosensory lateral line lobe by the electrosensory torus semicircularis of the midbrain in a mormyrid fish. The nucleus preeminentialis participates in an ascending pathway from the electrosensory lateral line lobe to the electrosensory torus as well as in feedback loop from the torus to the electrosensory lateral line lobe. An additional feedback pathway involves the inferior olive. The pathway between the torus and the nucleus preeminentialis is shown with a question mark because of some uncertainty about its existence.

located in the isthmus region, receives a major input from the electrosensory lateral line lobe and probably the electrosensory region of the **torus semicircularis**, which is part of the midbrain tectum in electrosensory fishes. The electrosensory torus has been reported to project back to the nucleus preeminentialis, although one recent study failed to confirm this connection. The nucleus preeminentialis then sends its axons back to the electrosensory lateral line lobe. A second feedback loop passes from the electrosensory torus semicircularis to the inferior olive to the caudal lobe of the cerebellum and finally back to the electrosensory lateral line lobe. Thus, the nucleus preeminentialis participates in two feedback loops to the electrosensory lateral line lobe: a direct loop and an indirect loop via the electrosensory torus semicircularis.

The circuitry of the teleost electrosensory system is quite complex and beyond the scope of an introductory text. Students with a need for more detailed information should consult the comprehensive work by Nieuwenhuys et al. (1998), which appears in the list of recommended readings at the end of the chapter, as well as the current literature.

CEREBELLAR EFFERENTS AND THE DEEP CEREBELLAR NUCLEI

In most groups of vertebrates, the sole pathway out of the cerebellar cortex is via the Purkinje cell axons. The two main targets of these axons generally are one or more cellular populations located within the cerebellar white matter or in the body of the pons and nuclei of the vestibular system. As described above, ray-finned fishes lack deep cerebellar nuclei; instead, the eurydendroid cells, which provide the efferents from the cerebellar cortex in these animals, pass directly to the vestibular nuclei, spinal cord, and other targets of the cerebellar cortex.

One or more deep cerebellar nuclei appear in lampreys, sharks, ropefishes (see Fig. 4-6), lungfishes, *Latimeria* (see Fig. 4-11), and amphibians. Reptiles have two nuclei (a **medial** and a **lateral**), and birds and mammals have three nuclei (a medial, a lateral, and an **interposed nucleus**). The medial nucleus of

BOX 14-3. Myelinated Dendrites in the Electrosensory Lateral Line Lobe of Mormyrids

Myelin is a form neural ensheathment that we ordinarily associate with axons. Recently, Johannes Meek and his colleagues described a unique situation in the electrosensory lateral line lobe of the mormyrid fish, *Gnathonemus petersii*. The electrosensory lateral line lobe, which is a cerebelloid structure, plays an important role in the detection of electric discharges of the fish's own electric organs. Meek et al. reported that the large multipolar cells of the lobe's intermediate cell and fiber layer give rise to dendrites that are covered with a myelin sheath (Fig. 1). These myelinated dendrites then enter, both contralaterally and ipsilaterally, the superficial and deep granule cell layers of the electrosensory lateral line lobe where they exhibit presynaptic

specializations that are indistinguishable from those of axon terminals. In spite of these presynaptic dendritic specializations, there are no corresponding postsynaptic specializations. Meek et al. raised the intriguing possibility that the myelinated dendrites may be stimulated by *ephaptic* contact; i.e., the myelinated dendrites are stimulated by the electrical fields generated around the granule cell axons, which in turn result in action potentials being generated in the multipolar cell's axon. Because the axons of these large, multipolar cells are GABAergic and also terminate in the granule cell layer, this hypothesized ephaptic stimulation would provide an extremely rapid, negative feedback loop to the granule cells.

Because the dendrites of these large multipolar cells are myelinated, they are only stimulated through the soma, which responds strongly to electrosensory stimulation, although they do not receive direct axon terminals from the fish's electroreceptors. Since the only known terminations of the mormyromast electroreceptors are on the granule cells of the superficial and deep granular layers of the electrosensory lateral line lobe, in which the myelinated dendrites are situated, the granule cells would seem to be the source of the stimulation to the multipolar cells. These terminations are both excitatory chemical and electrical gap junctions.

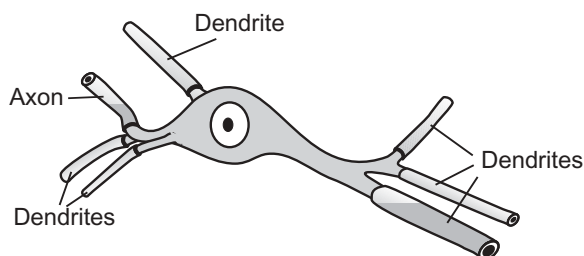


FIGURE 1. A large multipolar cell from the electrosensory lateral line lobe of a mormyrid fish. The light gray tubes at the end of the cell's processes represent myelin. Adapted from Meek et al. (2001) and use with permission of John Wiley & Sons.

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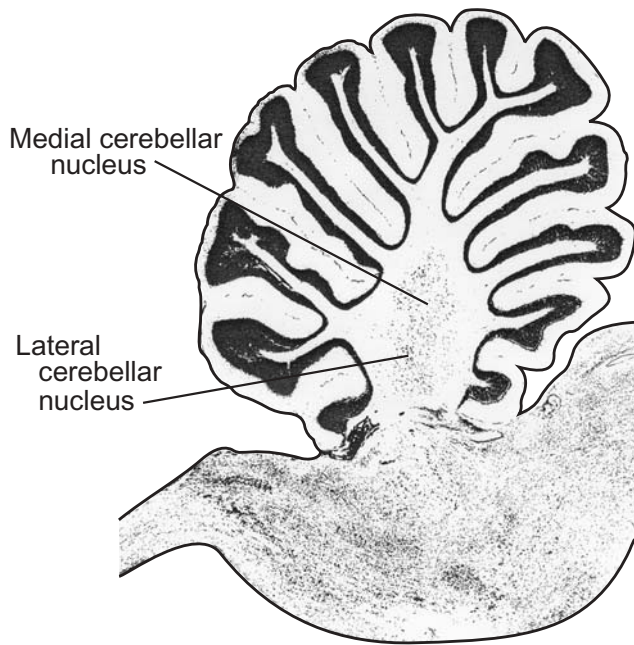


FIGURE 14-22. A parasagittal section through the hindbrain and cerebellum of a pigeon showing two of its three deep cerebellar nuclei. The nucleus cerebellaris internus is medial to the plane of this section and thus does not appear here. Adapted from Karten and Hodós (1967) and used with permission of The Johns Hopkins Press.

mammals is known as the **fastigial nucleus**, and the lateral nucleus is known as the **dentate nucleus**. The nucleus interpositus has an anterior division known as the **nucleus globosus** and a posterior division known as the **nucleus emboliformis**. The greater number of cerebellar nuclei in birds and mammals may be related to the greater lateral expansion and foliation of the cerebellum in these classes as well as the presence of a more elaborate system for telencephalic control of descending spinal and bulbar pathways. Two of the three deep cerebellar nuclei in a bird (pigeon) are shown in Figure 14-22.

In tetrapods, the Purkinje cells are organized into four longitudinal bands or zones according to the targets of their axons. In reptiles, the most medial band, band A, projects to the medial cerebellar nucleus. The next band, B, projects to the vestibular nuclei, followed by a band projecting to the lateral cerebellar nucleus, band C, and the fourth band, D, which projects to the vestibular nuclei. In mammals, band A projects to the medial (fastigial) cerebellar nucleus, band B to the lateral vestibular nucleus (Deiter's nucleus), band C to the two divisions of the nucleus interpositus, and band D to the lateral (dentate) cerebellar nucleus. Birds appear not to have a D band.

The efferents of the cerebellar nuclei (Fig. 14-23) can be classified into two general groups: those that ultimately affect motor neurons of the spinal cord and those that ascend to those neurons of the thalamus that are involved in motor function. In mammals, the major efferent pathway is the **superior cerebellar peduncle** or **brachium conjunctivum**. It arises from both the lateral (dentate) and interpositus nuclei. One of its major targets is the nucleus ruber (red nucleus) of the mid-

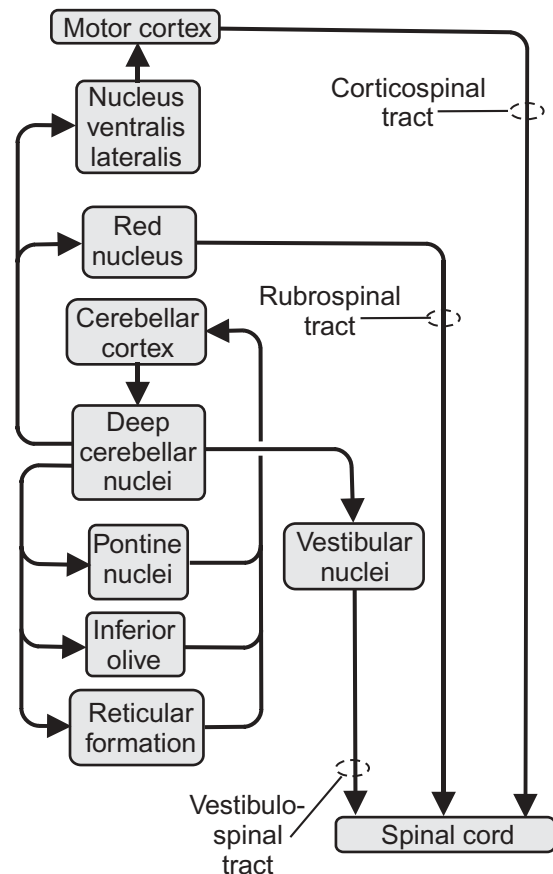


FIGURE 14-23. A summary of the major efferent pathways from the cerebellar cortex and deep cerebellar nuclei that affect the activity of spinal cord motor neurons in mammals. The main influences on spinal motor neurons are via the pathway to the red nucleus and the rubrospinal tract and via the thalamocortical route to the nucleus ventralis lateralis and motor cortex and then via the corticospinal tract. Other cerebellar influences on spinal motor neurons are via the vestibulospinal pathway and, not included in this figure, the reticulospinal pathway.

brain tegmentum, which in turn gives rise to the rubrospinal tract to the ventral horn of the spinal cord. The rubrospinal pathway influences the activity of spinal cord motor neurons that innervate flexor muscles, particularly of the upper limb. The second major target of the brachium conjunctivum is the dorsal thalamus, particularly nucleus ventralis lateralis, which in turn relays feedback information to motor-related areas of neocortex. The brachium conjunctivum also contains various other cerebellar efferent systems, including those to the reticular formation, pontine nuclei, inferior olivary nucleus, and hypothalamus, as well as a minor but direct projection to the spinal cord from nucleus interpositus.

A minor output pathway from the deep nuclei arises from the most medial of these nuclei, the fastigial nucleus. This pathway is the uncinate fasciculus, so named for its hook-like trajectory. The uncinate fasciculus is part of the inferior cerebellar peduncle; it distributes to the vestibular nuclei, as well as to the cervical spinal cord, and it also projects to the reticular formation and motor nuclei of the hindbrain.

Thus, direct cerebellospinal influences are few. The principal routes by which the cerebellum affects motor performance are via the descending rubrospinal and vestibulospinal tracts and by its ascending pathways to nucleus ventralis lateralis of the dorsal thalamus, which in turn influences motor regions of the telencephalon.

Regardless of the number of individual deep cerebellar nuclei, their efferents in nonmammals generally show the same pattern of distribution as in mammals. In reptiles and birds, the lateral cerebellar nucleus is the source of the brachium conjunctivum pathway to nucleus ruber and to the motor part of the dorsal thalamus, and the medial nucleus gives rise to the uncinate fasciculus pathway to vestibular nuclei and other brainstem cell groups.

EVOLUTIONARY PERSPECTIVE

The cerebellum is a structure of the brain that has had a seemingly paradoxical evolutionary history. On the one hand, it has maintained a rather conservative pattern in its cell types and the relationships of these cells to each other and to other cell populations within the brain. On the other hand, its gross structure shows extreme variations both within and between the vertebrate classes. The cerebellum thus illustrates both phyletic continuity and adaptation to the demands of the environment.

With regard to the cellular organization of the cerebellum, once the Purkinje cell assumed its two-dimensional, flattened dendritic tree, the main phyletic trends appear to have been (1) an early change in the role of the climbing fibers by having them climb the Purkinje cell dendrites rather than terminate on the soma, (2) a trend in the direction of refinement of inhibitory control over the granule cell/Purkinje cell circuitry by the addition of new inhibitory cell types in the tetrapods, and (3) the development and differentiation of multiple deep cerebellar nuclei in concert with the elaboration and expansion of the cerebellar hemispheres.

In contrast to the relative conservatism of the cerebellar circuitry, major changes have occurred in the overall form of the cerebellum. One such development has been the dramatic specializations in the valvula in mormyrids and other fishes with electroreception.

Other changes were related to the transition from water to land, as may be seen in the cerebella of extant amphibians and reptiles. As locomotor abilities advanced, along with the capacity to use the digits as organs of manipulation for digging, scratching, grasping, and carrying, the cerebellum showed dramatic lateral expansion and a massive increase in foliation, especially in mammals.

FUNCTIONS OF THE CEREBELLUM

A review of the literature on the functions of the cerebellum yields a bewildering array of seemingly unrelated responsibilities for this division of the central nervous system. Because of its afferent connections with the vestibular system and the somatosensory system and its efferent connections with the motor system, a major role of the cerebellum has long been

thought to be the maintenance of the balance of the body and the smoothness and coordination of muscular activity. In addition, a long series of studies also has suggested that the cerebellum plays a role in motor learning, and we have seen that, in fishes with electroreception, the cerebellum is a major sensory organ and possibly a cognitive organ as well. Some groups of neuroscientists have suggested a function of the cerebellum (and cerebelloid structures in general) is to process sensory expectations, i.e., to minimize the neural response to predictable stimulus events so that unpredictable events will be more detectable. A related proposal suggests that the cerebellum is involved in feedforward mechanisms that increase the accuracy of movements. Terms such as "feedback" and "feedforward" are derived from engineering control theory. The classic example of feedback is the thermostat that increases or decreases the activity of the heating system in response to changes in room temperature. Feedback is a reactive mechanism and can only make changes when an error is detected. Feedforward is a proactive mechanism that anticipates errors before they are made and prevents them from happening. This results in greater smoothness and accuracy in movements than would a system that relied only on a feedback process.

To understand the variety of functions that the cerebellum performs, one must look for a common denominator of all of these functions. One such common denominator is the organization of the cerebellar cortex into a very regular network of parallel fibers with Purkinje cells placed at regular intervals. This spatial arrangement seems well suited to the task of rather precise timing of events and for detecting the coincidence of events. The presence of several groups of specialized inhibitory cells limits the actions of the Purkinje and granule cells, which serve to enhance and sharpen the precision of this timing. Thus, the regulation and detection of temporal relations among events appear to be common themes among all of the known functions of the cerebellum. We are quite certain that neuroscientists have only begun to scratch the surface of the functions and behavioral capabilities of this fascinating brain structure.

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Part Three

THE MIDBRAIN

15

Overview of the Midbrain

INTRODUCTION

In all vertebrates, a group of structures collectively known as the midbrain, or mesencephalon, links the sensory, motor, and integrative components of the hindbrain with those of the forebrain. The midbrain contains three major regions: the **tectum**, the **tegmentum**, and the **isthmus** (Fig. 15-1). It should be noted that the word tegmentum is used generally for the more ventral part of the brainstem—e.g., midbrain tegmentum, isthmal tegmentum, or pontine tegmentum. In this text, we will use the word tegmentum to apply to the ventral part of the midbrain unless otherwise specified.

One important feature of the midbrain is the presence of areas within the tectum, or roof, that receive topographically organized projections from the auditory, visual, and somatosensory systems, which form maps of the animal's sensory space. Other features of the midbrain are the presence of nuclei intrinsic to the region and the presence of ascending and descending fiber tracts that pass through it. Finally, like the hindbrain, the midbrain also contains several nuclei that control the distribution of certain critical neurotransmitters to other brain regions. The tectum contains laminated structures—particularly the **optic tectum** and the **torus semicircularis**. The optic tectum receives its major input from the optic tract, which is the central continuation of the optic nerve. The optic tectum is involved in integrating the spatial aspects of visual and other sensory inputs and with spatially oriented motor responses. The torus semicircularis receives its major input from ascending auditory projections and, where present, from the lateral line system. The sensory maps in the midbrain roof are in register with each other; thus, visual and somatosensory

stimuli, for example, that arise from the same part of the space around the animal result in neuronal activity in the same part of the optic tectum. Auditory stimuli are mapped onto parts of the torus semicircularis that are interconnected in a point-to-point manner with parts of the optic tectum that likewise correspond in spatial register. Both the optic tectum and the torus semicircularis project rostrally to nuclei in the dorsal thalamus.

The main part of the midbrain tegmentum lies ventral to the tectum and is separated from the hindbrain by a transitional area called the isthmus, or isthmal tegmentum. Parts of the tegmentum consist of the rostral continuations of areas present in the hindbrain: the reticular formation, the oculomotor cranial nerve nuclei, and ascending and descending fiber systems. Additional nuclei, related to visuospatial functions, motor activities, ascending feedback for the integration and adjustment of motor activities, and relay to the forebrain of ascending sensory information, are also present. The midbrain tegmentum is thus a gateway for incoming sensory information and outgoing motor responses to and from the forebrain. It interacts with the more rostral parts of the brain for the analysis and modulation of the information.

In some species, especially in those with more laminar brains (Group I: see Chapter 4), not many experimental studies of connections have been done on tegmental nuclei. In these cases, we frequently do not yet know which populations of the cells that lie along the ventricular surface may project to a specific target and thus may correspond to particular nuclei in animals with more elaborated brains. Pinpointing these groups of cells must await future studies, but we need to note that a greater number of nuclei are present in these brains than can be identified for now. Specializations of nuclei and areas in the brainstem occur in correlation with the presence of specialized

capabilities such as electroreception, motor adaptation for specialized forms of swimming, and motor adaptations for locomotion on land. In this chapter, we will present a generalized overview of the structures and systems of the isthmus, the tegmentum, and the tectum.

For some of the nuclei in the avian midbrain, a new nomenclature recently has been introduced. This new set of terms was developed through extensive discussions among a number of avian and other comparative neurobiologists, and it was further honed and approved at The Avian Brain Nomenclature Forum, which was held at Duke University in July, 2002.

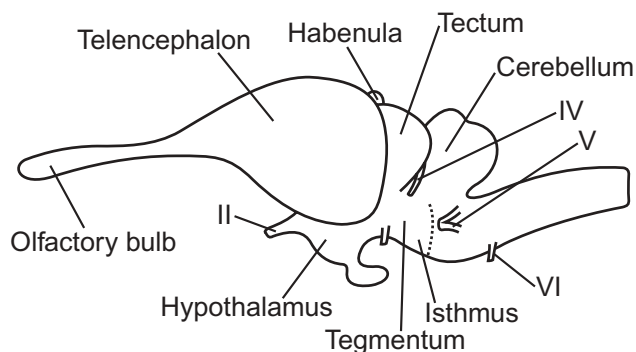


FIGURE 15-1. Lateral view of the brain of a crocodile, with the approximate caudal boundary of the isthmus indicated by a broken line. Cranial nerves are indicated by Roman numerals. Rostral is toward the left. Adapted from ten Donkelaar and Nieuwenhuys (1979) and used with the permission of Elsevier.

This new nomenclature employs the same terms as used in mammals in cases where homology is clear and compelling and neutral terms where it is not. The new terminology for avian midbrain nuclei is listed in Table 15-1.

THE ISTHMUS

The isthmus lies at the rostral end of the hindbrain. Within the isthmus are rostrally projecting cell groups, such as the locus coeruleus and raphe, the trochlear nucleus, and the rostral parts of some of the structures of the hindbrain, such as the reticular formation. A major ascending tract from the cerebellum, the brachium conjunctivum, is present as are numerous other ascending and descending fiber tracts. Some of these structures are shown in a sagittal view of a rat brain for orientation in Figure 15-2 and in a generalized, schematic diagram in Figure 15-3(A), which is an amalgamation of structures present in this region in various vertebrates. The relative positions of some isthmal structures are shown in a lamprey in Figure 15-4, a turtle in Figure 15-5, and a bird in Figure 15-6. A partial list of structures in the isthmus is given in Table 15-2.

The rostral part of the **reticular formation** extends into the isthmus and lies in its central part. The reticular formation (as discussed in Chapter 13) has widespread connections with a number of structures. It gives rise to the **reticulospinal tract**, which courses through the ventral part of the tegmentum and is important in motor control.

The **nuclei of the raphe** lie near the midline. Cells in the raphe contain the neurotransmitter **serotonin**. These cells, along with serotonin-containing cells located more rostrally in

TABLE 15-1. New Terminology for Selected Avian Midbrain Nuclei

Karten-Hodos (1967) or Other Previous Term	Karten-Hodos (1967) or Other Previous Abbreviation	New Latin Term	New Latin Abbreviation	New English Term	New English Abbreviation
Locus ceruleus-caudal part	Caudal LoC	Locus coeruleus	LoC	Locus coeruleus or A6	LoC or A6
Locus ceruleus-rostral part	Rostral LoC	—	—	A8	A8
Nucleus tegmenti pedunculopontinus pars compacta, except lateral edge	TPc, except for lateral edge	Substantia nigra pars compacta	SNC	Substantia nigra pars compacta or A9	SNC or A9
Lateral edge of TPc plus small area lateral to it (also previously called substantia nigra pars lateralis)	Lateral edge of TPc plus small area lateral to it	Substantia nigra pars reticulata	SNr	Substantia nigra pars reticulata	SNr
Area ventralis (of Tsai)	AVT	Area ventralis tegmenti	AVT	Ventral tegmental area or A10	VTA
Partly identified as nucleus profundus mesencephali pars ventralis	Partly identified as MPv	Nucleus pedunculopontinus tegmenti	PPT	Pedunculopontine tegmental nucleus	PPT

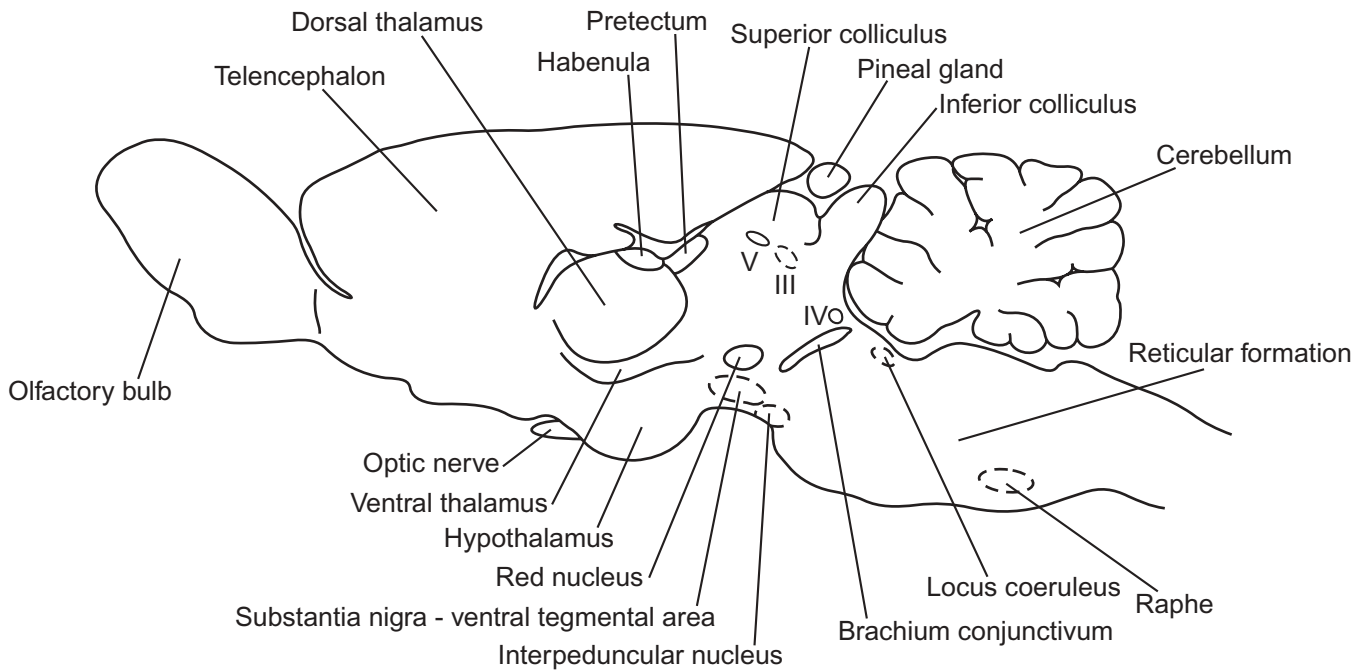


FIGURE 15-2. Drawing of a parasagittal section through the brain of a rat, showing the locations of some of the structures in the midbrain. Some nuclei, shown in broken lines, are out of the plane of section and have been projected onto this section to show their rostrocaudal and dorsoventral position relative to other structures. Cranial nerve nuclei are indicated by Roman numerals, with V indicating the mesencephalic nucleus of the trigeminal nerve. Adapted from Pelligrino et al. (1979) and used with kind permission of Springer Science and Business Media.

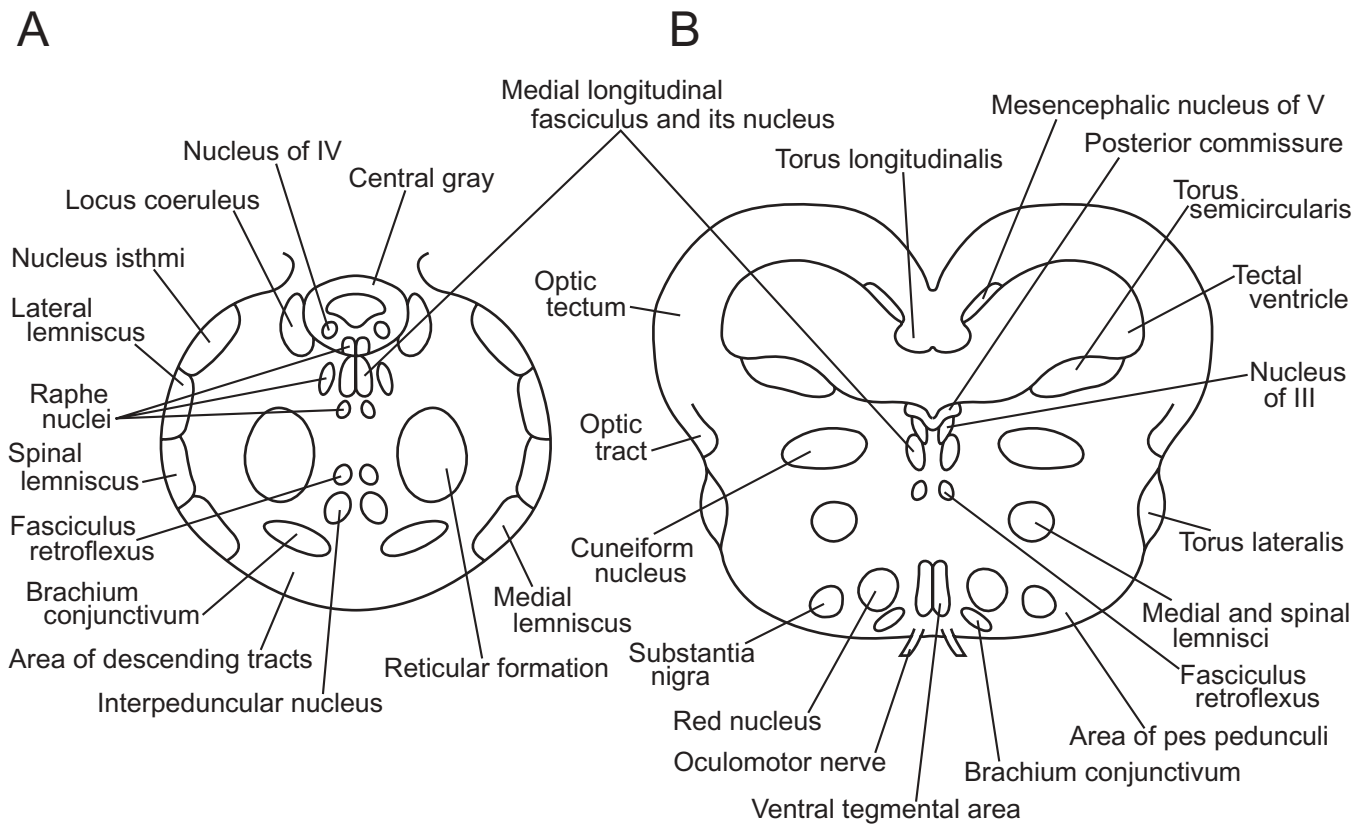


FIGURE 15-3. Schematic transverse sections through the isthmus (A) and the tegmentum and tectum (B) in a generalized vertebrate. The structures shown are not all present in any single species.

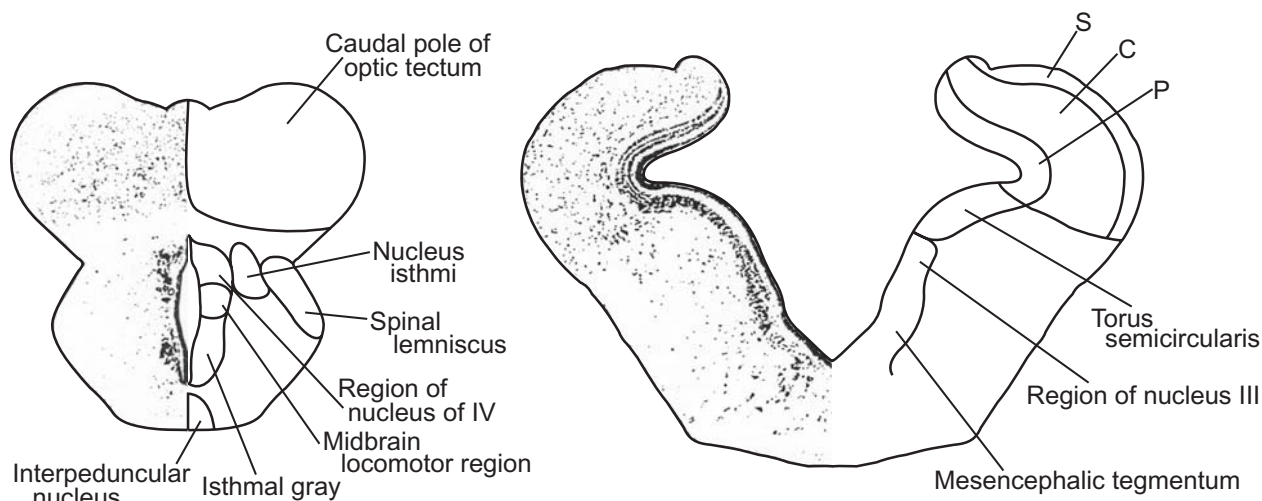


FIGURE 15-4. Transverse hemisections with mirror-image drawings through the midbrain of a lamprey. The more caudal section is on the left. Adapted from Kennedy and Robinson (1977) with additional data from Pombal et al. (2001). Note that, in this figure and in figures in this and succeeding chapters on the midbrain, the ventricle is either not labeled or is indicated by the abbreviation V. Used with permission of John Wiley & Sons.

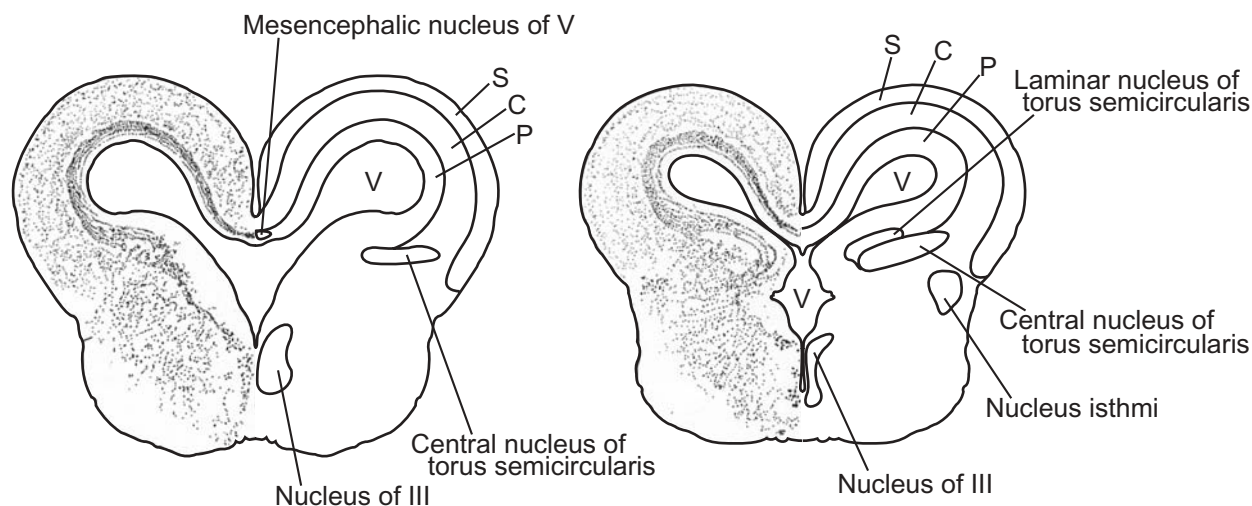


FIGURE 15-5. Transverse hemisections with mirror-image drawings through the isthmal region and tegmentum in a turtle (*Chrysemys scripta*). The more caudal section is on the left. Abbreviations: C, central zone of optic tectum; P, periventricular zone of optic tectum; S, superficial zone of optic tectum. Adapted from Browner et al. (1981) and used with permission of John Wiley & Sons.

FIGURE 15-6. Transverse hemisections with mirror-image drawings through the isthmal region and tegmentum in a pigeon (*Columba livia*). The more caudal section is at the top. In birds, tectal layers I through 12 have traditionally been regarded as forming the superficial zone, although only layers I through 8 correspond to the superficial zone of the reptilian tectum (see Chapter 18). Tectal layer 13 (or 9–13) form(s) the central zone, layer 14 is the deep white zone, and layer 15 is the periventricular gray. Adapted from Karten and Hodos (1967). Nissl photomicrographs used with permission of The Johns Hopkins University Press.

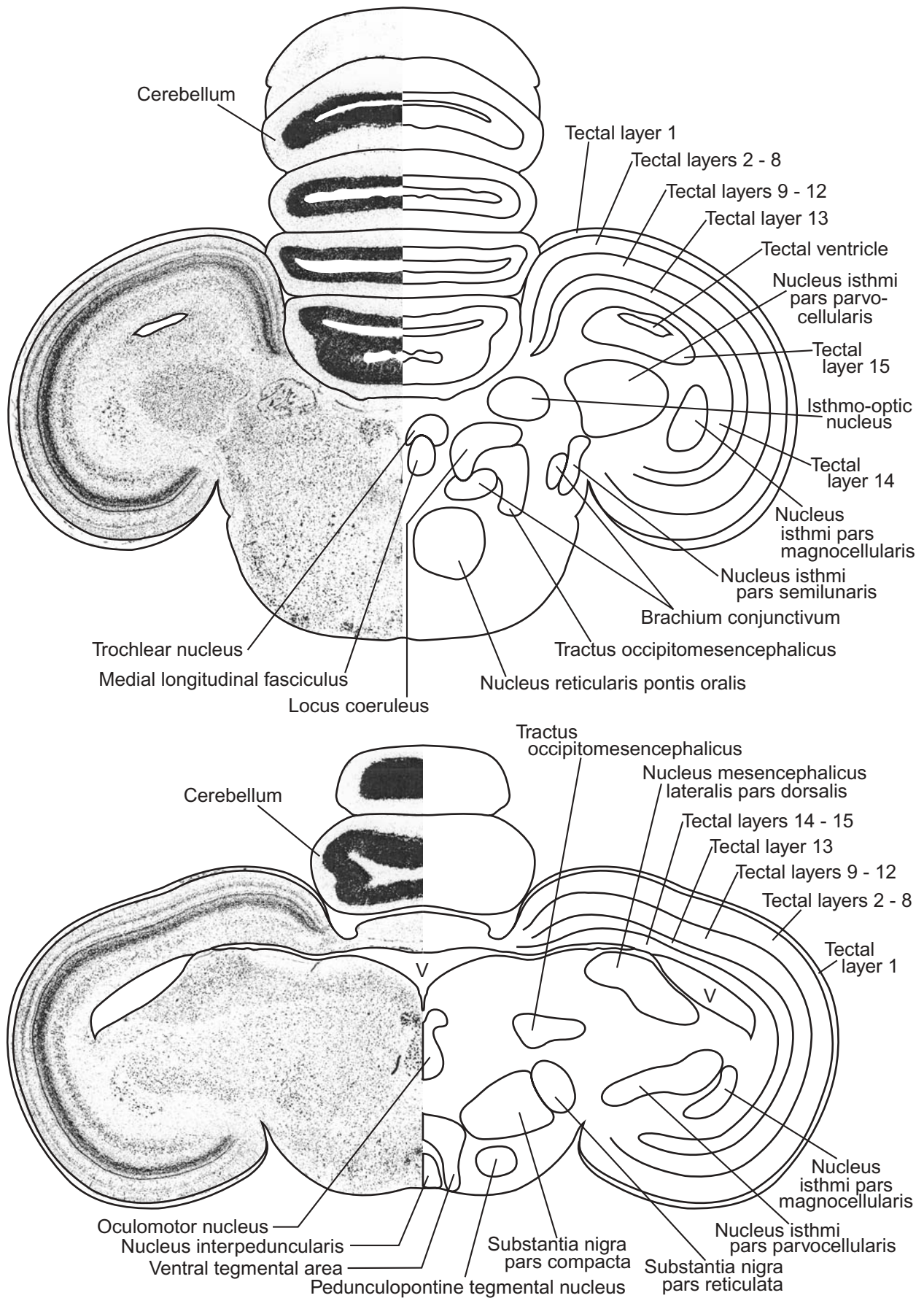


TABLE 15-2. Some of the Nuclei and Tracts in the Isthmus

Reticular formation	Motor, autonomic, and activating system
Nuclei of the raphe	Serotonin-containing cells that have widespread connections
Locus coeruleus	Catecholamine (norepinephrine)-containing cells that project to cerebral and cerebellar cortices
Trochlear nucleus	Nucleus of cranial nerve IV
Nucleus isthmi	Cholinergic cell group that is reciprocally connected with optic tectum
Isthmo-optic nucleus	Projects to the retina
Midbrain locomotor region	Integrates motor control circuits and projects to the reticular formation
Interpeduncular nucleus	Receives projections from the habenula in the diencephalon
Fasciculus retroflexus	Tract between habenula and interpeduncular nucleus
Brachium conjunctivum	Tract from cerebellum to red nucleus
Spinal lemniscus	Carries ascending pain and temperature information
Medial lemniscus	Carries ascending somatosensory information
Lateral lemniscus	Carries ascending auditory and lateral line information
Rubrospinal and reticulospinal tracts	Carry descending projections from red nucleus and reticular formation to spinal cord
Corticospinal, corticopontine, and other descending tracts	Carry descending projections from telencephalon to spinal cord and nuclei in the brainstem

the hypothalamus of the diencephalon, project to other brainstem nuclei, to motor cells in the spinal cord, to the optic tectum and other sensory processing structures, and to wide areas of the telencephalon. Serotonin has a variety of functions, including effecting the excitability of neurons in the forebrain. It plays a role in regulating mood and in perceptual integration and sleep.

The **locus coeruleus** is a nucleus that contains darkly pigmented cells bordering the central gray around the fourth ventricle. The cells are filled heavily enough with pigment to be visible to the unaided eye in fresh, unfixed tissue. Cells in the locus coeruleus contain the neurotransmitter **norepinephrine**, a catecholamine. Norepinephrine is present in some of the neuronal pathways that regulate movements and

in others that participate in cognitive functions and affect. The locus coeruleus projects to the pallium (including the cerebral cortex in mammals) in the telencephalon and to the cerebellar cortex.

The **trochlear nucleus**, which gives rise to cranial nerve IV, lies in the dorsal part of the tegmentum. It is interconnected with the oculomotor and abducens nuclei and with vestibular nuclei by the **medial longitudinal fasciculus**.

Nucleus isthmi is present in the isthmus in most vertebrates. It is called the **parabigeminal nucleus** in mammals. Nucleus isthmi is a collection of cholinergic neurons that is reciprocally connected with the optic tectum in a point-to-point manner so that the map of visual space in the tectum is also topographically represented in this nucleus.

An **isthmo-optic nucleus** is present in the dorsomedial part of the isthmal region [rostral to the level shown in Fig. 15-3(A)] in some vertebrates. Unlike nucleus isthmi, this nucleus does not have tectal connections. Neurons of the isthmo-optic nucleus project centrifugally to the retina.

An area called the **midbrain locomotor region** (MLR) lies in the central part of the tegmentum. Stimulation of parts of the MLR results in movements of the limbs. A prominent cholinergic cell group, the pedunculopontine nucleus, lies within the MLR and is one of its major components. Its main projections, particularly as studied in mammals, are ascending and serve to integrate cerebellar and striatopallidal circuits (see Chapter 24). In mammals, a nucleus called the **cuneiform nucleus** lies dorsal to the pedunculopontine nucleus and is also involved in motor functions. Its projections are mainly to reticular formation sites in the medulla, which in turn project to the spinal cord.

The **interpeduncular nucleus** lies in the ventral part of the isthmus. It receives descending projections from the habenula in the diencephalon, which receives input from olfactory and limbic related areas of the telencephalon. The tract between the habenula and the interpeduncular nucleus is the **fasciculus retroflexus**. The interpeduncular nucleus sends efferent projections to other areas within the dorsal part of the tegmentum.

The **brachium conjunctivum** is a tract that carries fibers from the contralateral cerebellum to the **red nucleus** in the tegmentum. The red nucleus projects to the spinal cord via the **rubrospinal tract**, which courses through the ventral part of the isthmus.

Ascending tracts carrying sensory information also course through the isthmus and tegmentum. The **spinal lemniscus**, a continuation of the lateral funiculus of the spinal cord, carries pain and temperature information. The **medial lemniscus** carries somatosensory information: touch, proprioception, and vibration senses. The **lateral lemniscus** carries ascending auditory projections in all animals and, in many, ascending electrosensory and/or mechanosensory lateral line projections.

The **corticospinal** and **corticopontine tracts** are large and prominent in mammals. These tracts arise in the cerebral cortex and form large structures called the **pes pedunculi** (see Chapter 17) on the lateral edge of the tegmentum. The term “interpeduncular nucleus” is derived from its position dorsal to the pes pedunculi and to the side of the **interpeduncular fossa**, which partially divides the two halves of the midbrain in mammals.

THE TEGMENTUM

The tegmentum lies ventral to the tectum in the midbrain. The tegmentum contains some cranial nerve nuclei—the oculomotor nucleus and the mesencephalic nucleus of the trigeminal—as well as other nuclei such as the cuneiform nucleus, substantia nigra, ventral tegmental area, and the red nucleus, which receives ascending cerebellar projections. Many ascending and descending tracts pass through or originate in the tegmentum. Some tegmental structures are shown in the sagittal view of a rat brain in Figure 15-2 and in the generalized, schematic diagram of a transverse section in Figure 15-3(B). Figures 15-4 through 15-6 show the relative positions of some tegmental structures in a lamprey, a turtle, and a bird, respectively. A list of a number of the structures in the tegmentum is provided in Table 15-3.

Large neurons of the mesencephalic nucleus of the trigeminal nerve (see Chapter 11) lie within the deep layers of the

optic tectum. These neurons receive proprioceptive information from jaw muscles and are part of a monosynaptic reflex arc for regulation of the movements of the muscles.

The **oculomotor nucleus** lies in the dorsal part of the tegmentum in a medial position. It gives rise to the oculomotor nerve, which courses ventrally through the tegmentum to exit the brain. The **red nucleus** lies immediately lateral to the fibers of the oculomotor nerve. The nucleus is so named because of its pinkish color, due to the presence of abundant blood vessels, in fresh specimens of some animals. It is a major target of the deep cerebellar nuclei and also receives descending projections from the telencephalon. Thus, the red nucleus can integrate and coordinate motor signals from both sources. The red nucleus projects to the spinal cord via the rubrospinal tract.

The **substantia nigra** and **ventral tegmental area** lie near the red nucleus. The cells of the ventral tegmental area and the pars compacta of the substantia nigra contain the catecholamine dopamine. They project to a number of sites in the diencephalon and telencephalon and are involved in the initiation and control of movements. In humans, loss of cells in the substantia nigra results in the tremors, rigidity, and other symptoms of Parkinson's disease. The substantia nigra has a second component, the pars reticulata, that comprises a population of GABAergic neurons. These neurons project to a rather wide array of targets, including the optic tectum.

The **medial longitudinal fasciculus** lies next to the oculomotor nucleus and, as discussed above, interconnects the oculomotor, trochlear, and abducens nuclei with vestibular nuclei. The **fasciculus retroflexus** is also present at this level, carrying fibers from the habenula to the interpeduncular nucleus in the isthmus.

The **brachium conjunctivum** projects to the red nucleus, carrying fibers from the cerebellum. The tract lies ventromedial to the nucleus, as its fibers enter the nucleus to terminate there. Other ascending tracts pass through the tegmentum on the way to the tectum and to nuclei in the diencephalon. These include the spinal lemniscus and medial lemniscus, which carry pain and somatosensory information as discussed above.

Tracts that descend through the tegmentum include the corticospinal and corticopontine tracts, present in mammals, which form the pes pedunculi on the lateral surface of the tegmentum, as well as corticoreticular fibers. Other descending tracts include corticonuclear projections to oculomotor nerve nuclei and corticobulbar projections to the rest of the motor cranial nerve nuclei. Fibers from a variety of sources cross to the contralateral side in the tegmentum via the **posterior commissure**. The **torus lateralis** is a bulge on the lateral side of the tegmentum that is present in ray-finned fishes but has not been identified in other vertebrates. It has been found to project to the telencephalon, but its other connections and functions are unknown.

Mesencephalic nucleus of the trigeminal nerve	Proprioception for jaw muscles; the cells lie in the deep part of the tectum
Oculomotor nucleus	Nucleus of cranial nerve III
Red nucleus	Receives cerebellar and descending projections and projects to spinal cord
Substantia nigra pars compacta	Catecholamine (dopamine)-containing cells that project to basal ganglia in the telencephalon
Substantia nigra pars reticulata	GABAergic neuron population that projects to multiple sites, including the optic tectum
Ventral tegmental area	Catecholamine (dopamine)-containing cells similar to those in substantia nigra
Medial longitudinal fasciculus	Interconnects oculomotor and vestibular nuclei
Fasciculus retroflexus	Tract from habenula to the interpeduncular nucleus
Brachium conjunctivum	Tract from cerebellum to the red nucleus
Spinal lemniscus	Carries ascending pain and temperature information
Medial lemniscus	Carries ascending somatosensory information
Corticospinal and corticopontine tracts	Carry descending information from the telencephalon
Posterior and tectal commissures	Carry a variety of decussating fibers
Torus lateralis	Connections mostly unknown

THE TECTUM

The two prominent structures within the tectum are the **optic tectum** and **torus semicircularis**. These two structures occur in all vertebrates and form rounded bulges over the

tegmentum. In mammals, they are called the **superior colliculus** and **inferior colliculus**, respectively. Colliculus is Latin for “little hill,” which each bulge resembles. A third structure—the **torus longitudinalis**—is present at the medial edge of the optic tectum in ray-finned fishes (see Chapters 14 and 18). The optic tectum, torus semicircularis, and torus longitudinalis are shown schematically in Figure 15-3(B).

The optic tectum is formed by a lobe on each side of the brain (Figs. 15-1 through 15-6). It is most properly called by its full name, to distinguish it from the entire midbrain roof, but is also referred to simply as the tectum in some contexts. In many nonmammalian vertebrates, the optic tectal lobes are relatively expanded, and the ventricular space extends laterally into each tectal lobe, forming the tectal ventricle. The optic tectum consists of various layers of cells and fibers, with the dendrites of many cells oriented in a radial fashion and with afferent fibers coursing through it parallel to the surface. The cell and fiber layers can be divided into superficial, central, and periventricular zones. The optic tectum has multiple sources of input, among which are the visual and somatosensory systems. The optic tract terminates in the superficial and central zones, while somesthetic information terminates in the deeper part of the central zone. The inputs of both of these modalities are mapped topographically and are in register with each other in regard to their spatial location of origin. There is a **tectal commissure** interconnecting the optic tecta, although in a number of taxa it contains few if any tectotectal fibers.

As a result of the expansion of the tectal lobes, the torus semicircularis lies ventral to the tectal ventricle in most cases (Figs. 15-3–15-5). In birds, in which it is called **nucleus mesencephalicus lateralis pars dorsalis** (Fig. 15-6), it also lies ventral to the tectal ventricle. In mammals, the inferior colliculus lies caudal to the superior colliculus, rather than in a more ventral position, because the superior collicular lobes are not expanded laterally and the ventricle does not extend into them.

The torus semicircularis is the site of termination of auditory and lateral line fibers from the lateral lemniscus. The topography of these fibers is maintained so that there is a map of lateral line and/or auditory space in the torus semicircularis. The torus semicircularis is also reciprocally connected with the optic tectum, and the maps of visual and somatosensory space in the optic tectum and of auditory/lateral line space in the torus semicircularis are maintained in register in both structures. Descending projections involved in motor movements to orient the head and/or body to novel stimuli in the environment arise from both the optic tectum and the torus semicircularis, and the mapping of space allows for rapid and precise orienting movements. This is equally important to a frog needing to catch a fly for lunch as to a human orienting to “things that go bump in the night” (as the traditional Scottish prayer puts it) or to an unexpected motion in one’s peripheral

visual field. In addition to descending projections, the optic tectum and the torus semicircularis both project rostrally to nuclei in the diencephalon, which in turn project to the telencephalon.

The torus longitudinalis is a small structure that is unique to ray-finned fishes (see Fig. 16-2). As discussed in Chapters 14 and 18, it is part of a descending visual pathway to the optic tectum and corpus cerebelli.

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16

Isthmus

INTRODUCTION

We have previously discussed a number of isthmic nuclei and tracts, such as the reticular formation, the trochlear and oculomotor nuclei, and the medial longitudinal fasciculus. Other tracts that pass through the midbrain tegmentum and the isthmus, including the medial and spinal lemnisci and a number of the descending tracts, are also covered elsewhere in conjunction with the specific systems to which they belong. This chapter focuses on the region called the isthmus. The word *isthmi* refers to a narrow connecting part or neck. Here we will consider the comparative anatomy of six isthmal structures: the **nuclei of the raphe**, the **locus coeruleus**, **nucleus isthmi**, the **isthmo-optic nucleus**, the **midbrain locomotor region (MLR)**, and the **interpeduncular nucleus**. The raphe nuclei and locus coeruleus also were discussed in Chapter 13 as part of the reticular formation.

Drawings of sections through the isthmus show a number of the nuclei and fiber tracts for a variety of animals with laminar brains (Group I)—a lamprey (Fig. 16-1), a nonteleost ray-finned fish (Fig. 16-2), a lungfish (Fig. 16-3), and an amphibian (Fig. 16-4)—and for some animals with elaborated brains (Group II)—a hagfish (Fig. 16-5), a skate (Fig. 16-6), a teleost (Fig. 16-7) and, among amniotes, a mammal (Fig. 16-8) and a bird (Fig. 16-9). The isthmal region in a turtle is shown in Figure 15-5.

NUCLEI OF THE RAPHE

Group I

In most vertebrates, the nuclei of the raphe extend into the isthmus. In lampreys, the raphe has cells that contain sero-

tonin but is confined to the hindbrain proper, even though this system is quite extensive within the hindbrain. It gives rise to widely distributed projections to the telencephalon, diencephalon, tectum, interpeduncular nucleus, and reticular formation. In squalomorph sharks and ratfishes, the raphe lies dorsal and caudal to the interpeduncular nucleus. The raphe nuclei in ratfishes are known to have serotonin-containing cells. These cells are also distributed through more lateral areas within the brainstem.

Among nonteleost ray-finned fishes, the serotonin system in the raphe is known to be extensive in sturgeons and gars. In the latter, it extends caudally to upper spinal cord levels; in the isthmus (Fig. 16-2), the area of the serotonin-containing cells extends lateral to the raphe itself.

Differences occur in the degree of lateralization of this system in amphibians. In frogs, the serotonin-containing cells of the raphe extend from medullary to isthmic tegmental levels in the area of the midline and also extend into more lateral areas in the tegmentum. In urodele amphibians, however, the serotonin-containing cells are confined to the raphe nuclei in the area of the midline.

Group II

In hagfishes, the nucleus of the superior raphe extends rostrally to the level of the caudal isthmus (Fig. 16-5). Serotonin-containing cells are mostly confined to the area of the midline. In galeomorph sharks, skates, and rays, the rostral part of the raphe also extends into the isthmus, a part of it lying dorsal to the caudal part of the interpeduncular nucleus. Serotonin-containing cells are numerous within the raphe and also are distributed through a number of more laterally lying sites in the hindbrain.

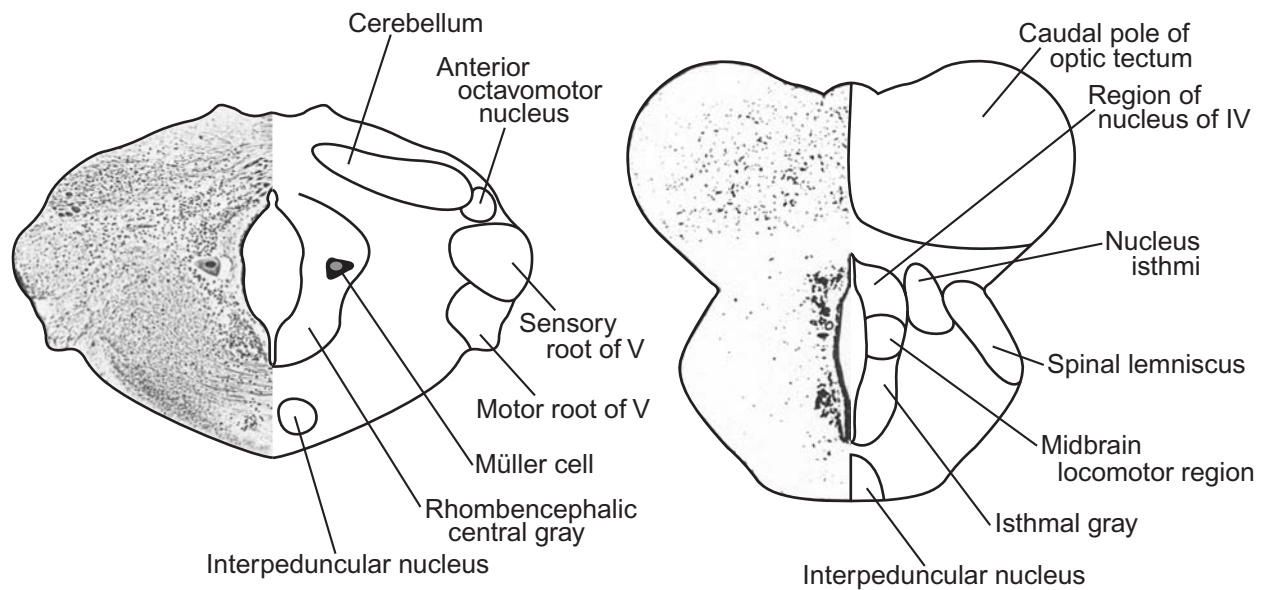


FIGURE 16-1. Transverse hemisections with mirror-image drawings through the level of the isthmus in the lampreys *Ichthyomyzon unicuspis* (left) and *Petromyzon marinus* (right). These hemisections are adapted from Northcutt (1979) and Kennedy and Robinson (1977), respectively, with additional identification of cell groups in *Ichthyomyzon* after Nieuwenhuys et al. (1998). The section for *Ichthyomyzon* is more caudal, and its Nissl photomicrograph is used with permission of Elsevier. The section for *Petromyzon* is used with permission of John Wiley & Sons.

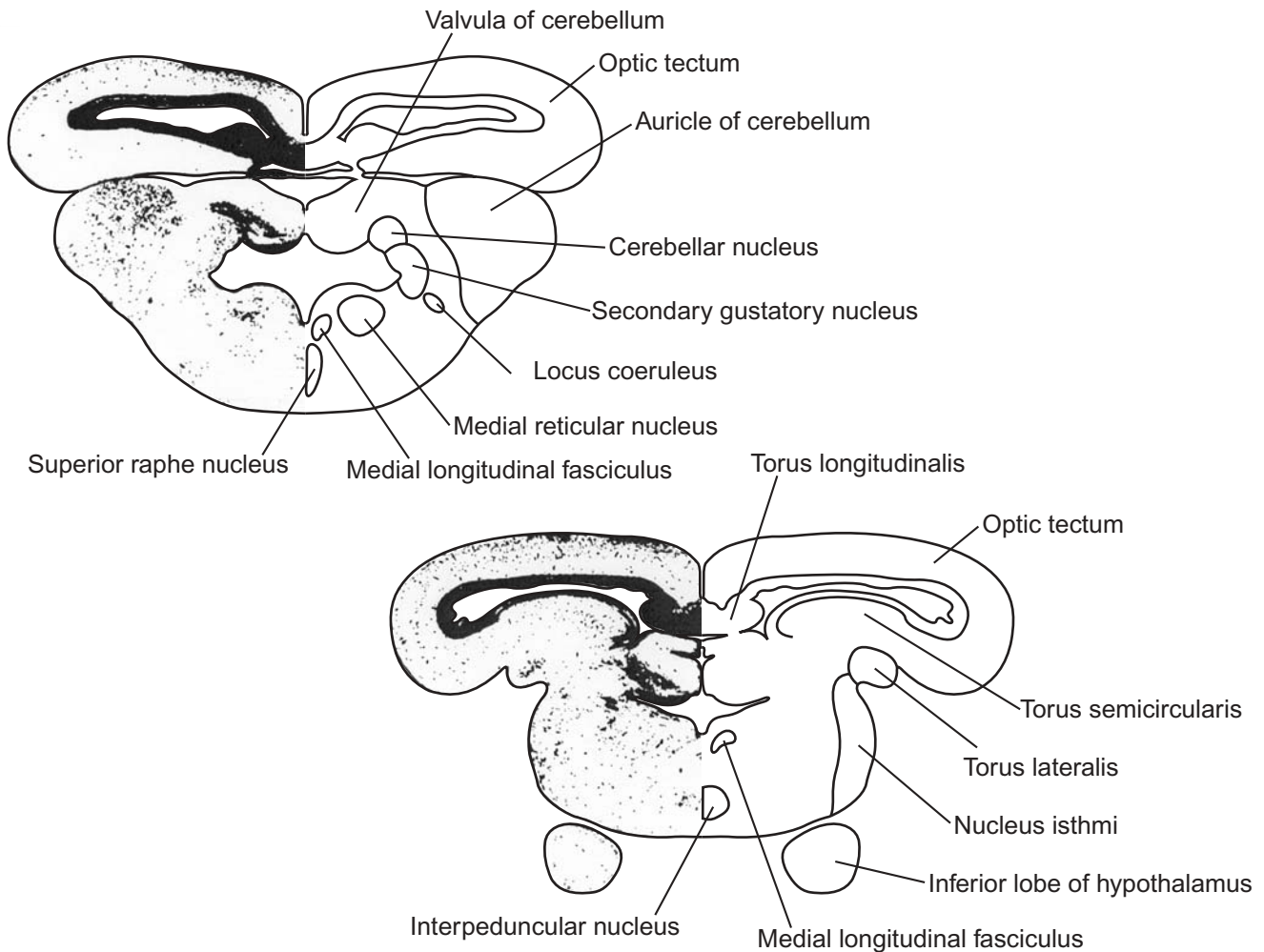


FIGURE 16-2. Transverse hemisections with mirror-image drawings through isthmal levels in a long-nose gar (*Lepisosteus osseus*), with the more caudal section at the top. Adapted from Northcutt and Butler (1980). Used with permission of Elsevier.

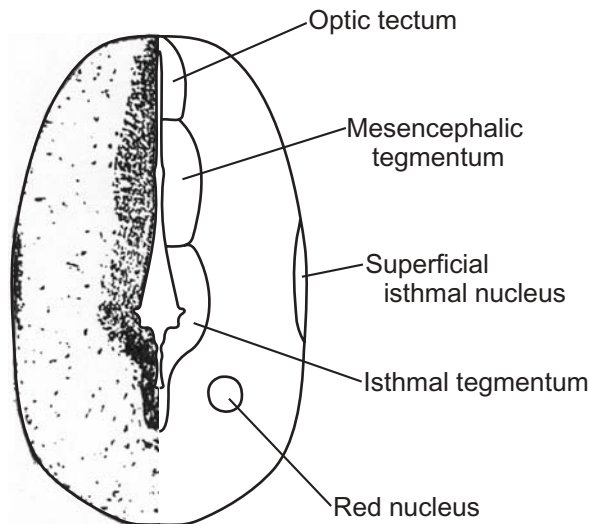


FIGURE 16-3. Transverse hemisection with mirror-image drawing through the isthmus in a lungfish (*Protopterus annectens*). Adapted from Northcutt (1977) with additional data from Northcutt and Ronan (1985). Used with permission of John Wiley & Sons.

The column of the raphe nuclei extends into the caudal part of the isthmus in teleosts (Fig. 16-7). The medially lying raphe nuclei have serotonin-containing cells, but this system is relatively limited in teleosts. The column of serotonin-containing cells in the raphe does not extend caudally through the medulla and into the spinal cord in most teleosts as it does in lampreys, cartilaginous fishes, and nonteleost ray-finned fishes such as gars. One exception to the limited extent of the system in teleosts is in mormyrid fishes where serotonin-containing cells extend throughout the brainstem. In most teleosts, the serotonin-containing cells are also limited in their lateral extent, being confined to the area of the midline. This lack of lateral migration of the cells contrasts with the more laterally migrated reticular formation and a number of other nuclei in teleosts.

In amniotes (Fig. 16-8), the serotonin-containing cells lie both within the nuclei of the raphe and more laterally in the tegmentum. This lateralization of the serotonin system is pronounced in mammals and most extensive in birds. In both mammals and birds, some serotonin-containing cell somata extend as far laterally as nuclei such as the locus coeruleus (discussed below), where they intermingle with the catecholamine-containing cells of that region. The number of such intermingling serotonin-containing cells is relatively few in mammals but quite high in birds. The functional consequences of having the cell somata intermingled have not yet been determined.

In mammals, widespread ascending serotonergic projections of the raphe have been found to the cerebral cortex in the telencephalon, nuclei within the diencephalon, the superior colliculus in the roof of the midbrain, and the cerebellum. These projections have also been found to be topographically organized.

Evolutionary Perspective

The serotonin system is well developed and extends laterally from midline areas in most vertebrates. Hagfishes, teleosts, and urodele amphibians are the exceptions, having relatively reduced systems in which the cells are confined to the area of the midline. Although we cannot determine whether lateralization of the serotonin system was present in the common ancestor of hagfishes and all other vertebrates, this condition does appear to have arisen very early in vertebrate evolution. Lateralization of the system has been maintained in most groups and, in some cases, augmented. The system has been secondarily reduced in teleosts and in urodele amphibians.

LOCUS COERULEUS

Group I

The presence of a locus coeruleus, which means “sky-blue place” in reference to the color of its catecholamine-containing cells, has not yet been identified with certainty in lampreys, but, among cartilaginous fishes, this nucleus has been found in ratfishes along the border of the fourth ventricle. In nonteleost ray-finned fishes such as sturgeons and gars, the locus coeruleus is a small group of catecholamine-containing cells (shown in the top section in Fig. 16-2) in the isthmus, and within the telencephalon, there are only a few catecholamine-containing axons. The locus coeruleus is thus quite small, especially in contrast to the extensive serotonin system of the raphe. In amphibians, the catecholamine-containing cells of the locus coeruleus lie on the ventromedial wall of the fourth ventricle.

Group II

The presence of a locus coeruleus has not yet been investigated in hagfishes. Among cartilaginous fishes with elaborated brains, a circumscribed group of cells forms the locus coeruleus in galeomorph sharks, lying in the caudal part of the isthmus along the border of the fourth ventricle. This nucleus has not yet been identified in skates, but a locus coeruleus with scattered, catecholamine-containing cells has been found in a closely related animal, the guitarfish, caudal to the isthmus at the level of the trigeminal motor nucleus. The locus coeruleus projects to the spinal cord, cerebellum, and telencephalon. In teleosts, the locus coeruleus (Fig. 16-7), with numerous, large catecholamine-containing cells, lies dorsal to the reticular formation. In contrast with the serotonin system, the locus coeruleus is larger in teleosts than in nonteleost ray-finned fishes, and there is dense innervation of a number of areas within the midbrain and forebrain, including part of the telencephalon, by catecholamine-containing fibers.

In amniotes, the locus coeruleus lies along the lateral edge of the rostral end of the fourth ventricle (Figs. 16-8 and see Fig. 15-6). The locus coeruleus in birds is a smaller group of cells than previously designated in the Karten and Hodos atlas of the pigeon brain and subsequent atlases in other species. It comprises only the cells in the caudal half of the nucleus as previously identified. The noradrenergic, locus coeruleus cell

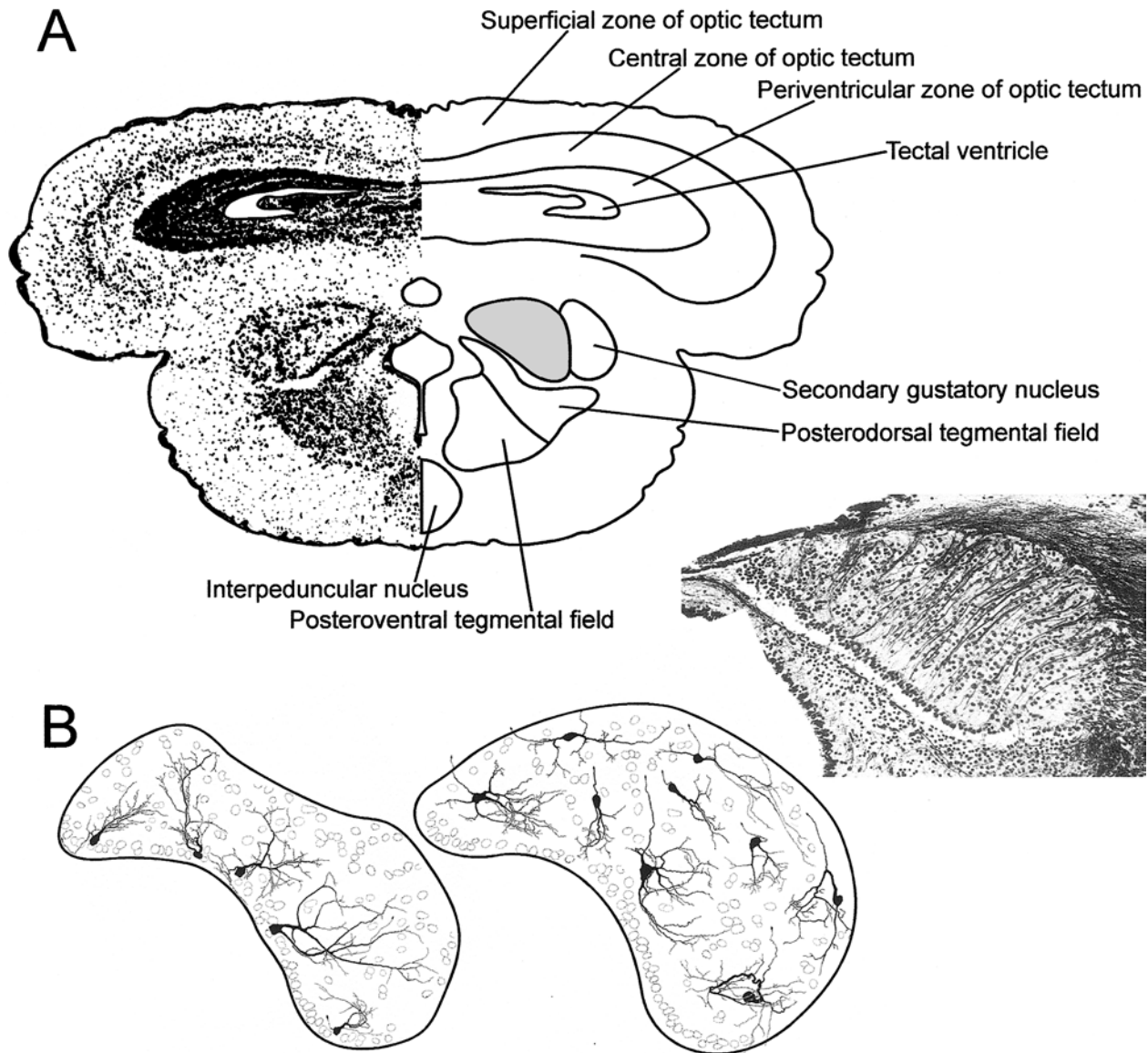


FIGURE 16-4. Transverse hemisection with mirror-image drawing through the isthmus (A) in a leopard frog (*Rana pipiens*), with an enlarged photomicrograph through nucleus isthmi to the lower right, stained with the Klüver-Barrera method for cells and fibers. Nucleus isthmi is indicated in the line drawing by shading. Camera lucida drawings (B) of cortical-type (left) and medullary-type (right) neurons in nucleus isthmi of *Xenopus laevis*. The Nissl photomicrograph in A is adapted from Wilczynski and Northcutt (1977), and the Klüver-Barrera section is from Gruberg et al. (1994). The neuron drawings in B are from Tóth et al. (1994). All parts of this figure used with permission of John Wiley & Sons.

population in birds laterally borders the fourth ventricle only at rostral pontine levels. (The more rostral part of what was previously identified as locus coeruleus in birds is actually a dopaminergic cell group.) In all amniotes, the noradrenaline-containing cells of the locus coeruleus project topographically to various parts of the forebrain, midbrain, hindbrain, and spinal cord. Like the serotonin-containing neurons of the raphe, the locus coeruleus plays a role in affecting the activity of sensory neurons and the general level of activity of the pallium in the telencephalon.

Evolutionary Perspective

A locus coeruleus is a common feature of the brains of jawed vertebrates. Regardless of whether it is also present in lampreys and hagfishes, we can conclude that this group of catecholamine-containing cells with widespread projections evolved early in vertebrate history.

In some cases, this set of cells seems to be developed in inverse proportion to the serotonin system of the raphe. In nonteleost ray-finned fishes, the locus coeruleus is relatively

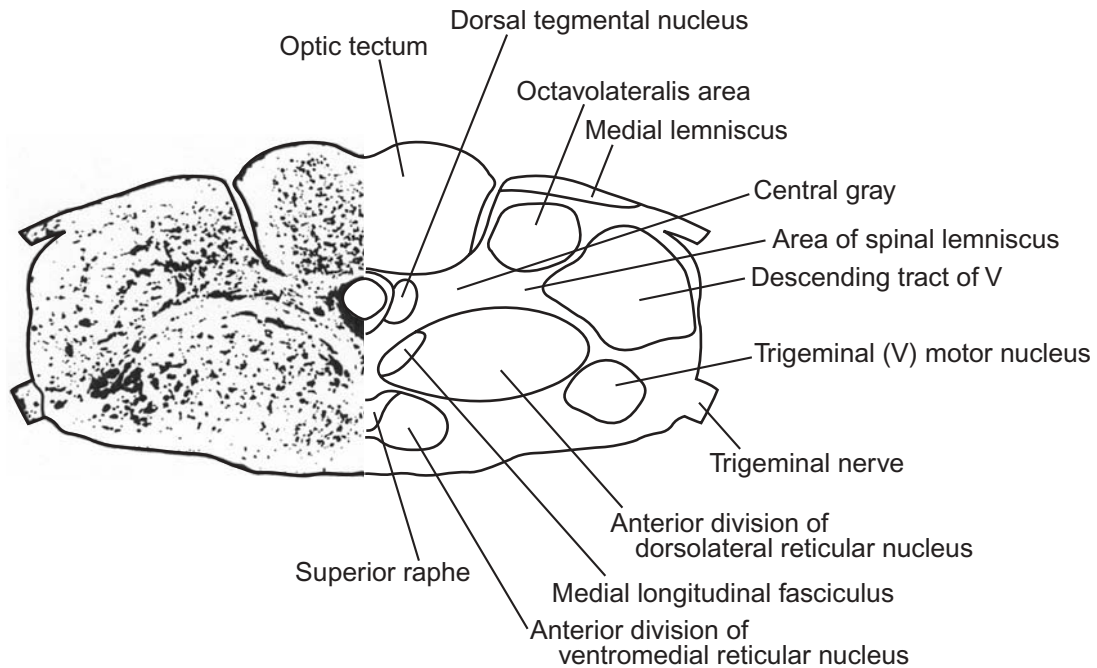


FIGURE 16-5. Transverse hemisection with mirror-image drawing through the isthmus in a hagfish (*Eptatretus stouti*). Adapted from Ronan and Northcutt (1990) and used with permission of John Wiley & Sons.

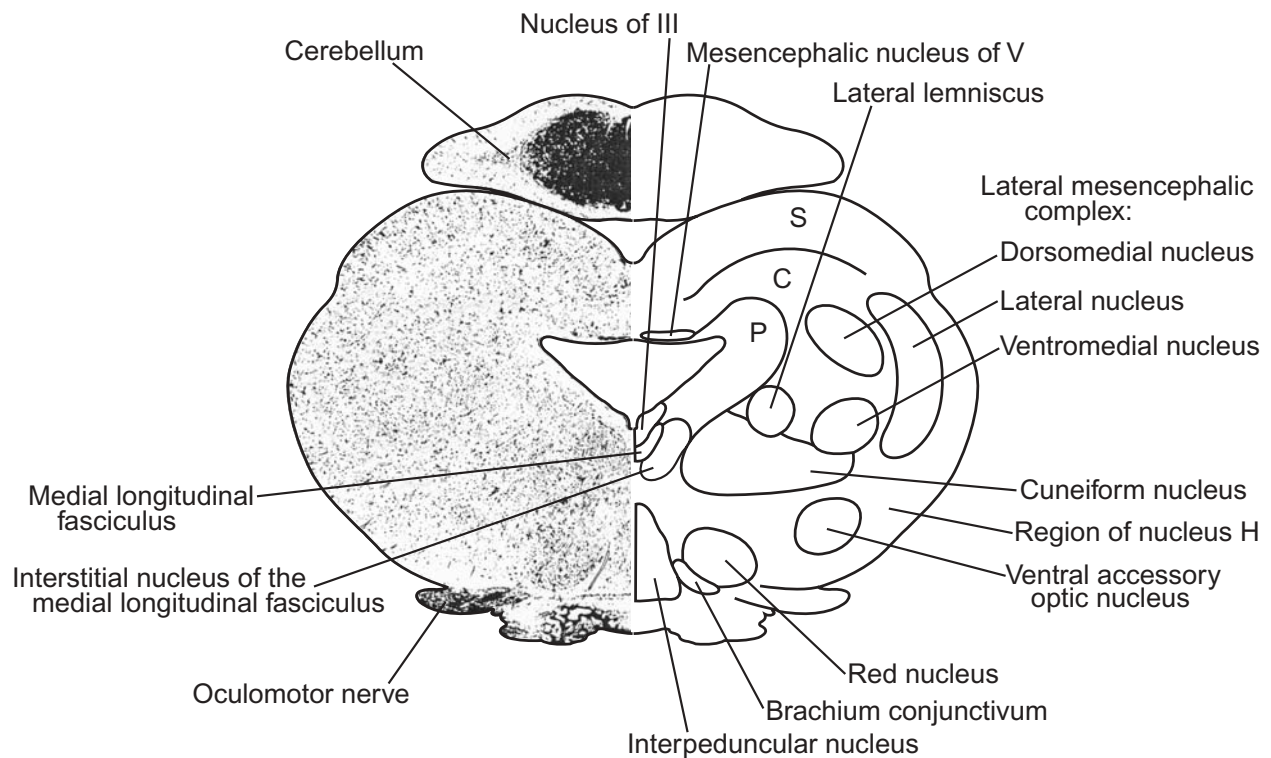


FIGURE 16-6. Transverse hemisection with mirror-image drawing through the isthmus of a skate (*Raja eglanteria*). Adapted from Boord and Northcutt (1982) and used with permission of John Wiley & Sons.

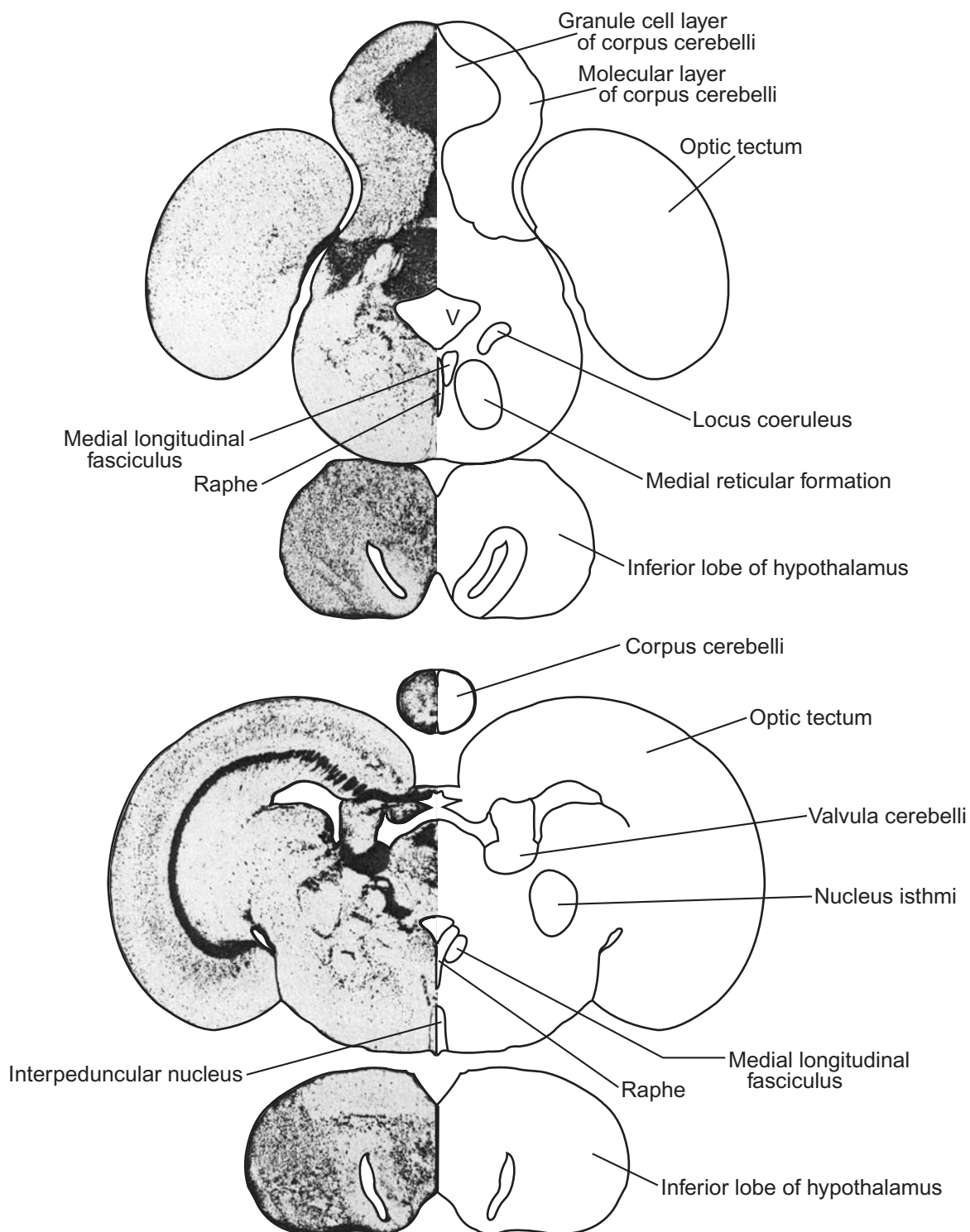


FIGURE 16-7. Transverse hemisections with mirror-image drawings through the isthmus in a teleost (*Lepomis gibbosus*), with the more caudal section at the top. Adapted from Parent et al. (1978) and used with permission of John Wiley & Sons.

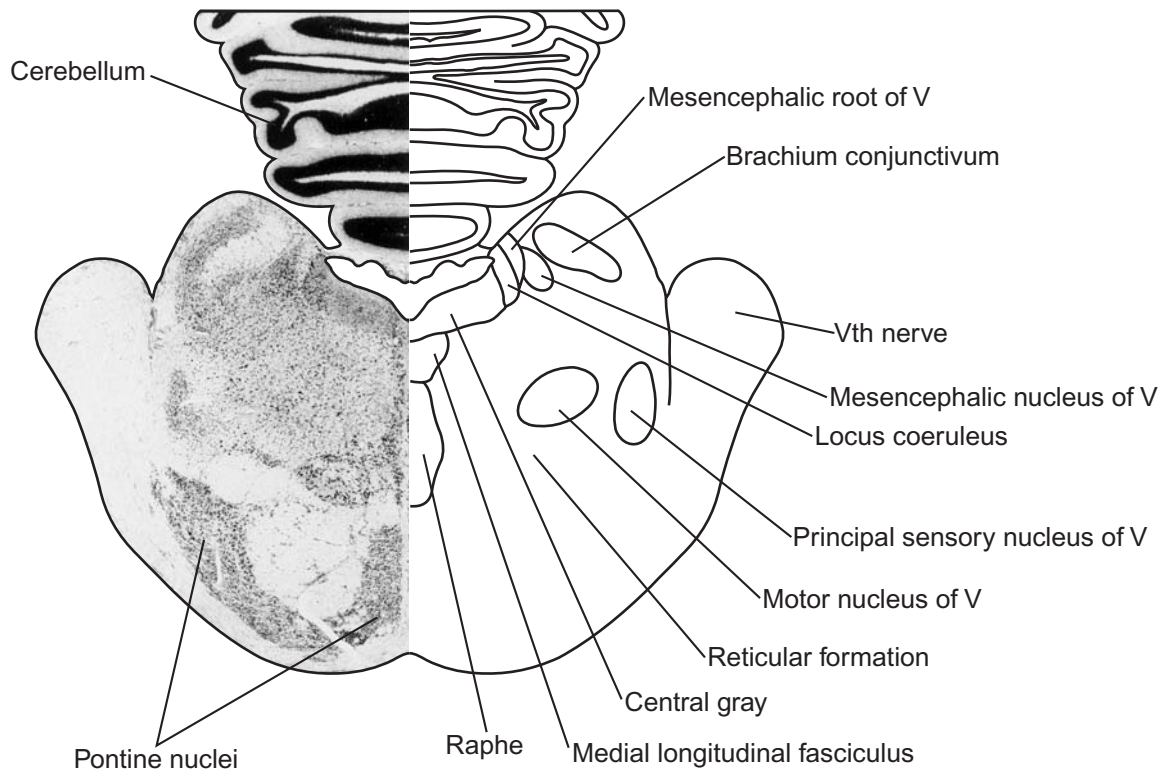


FIGURE 16-8. Transverse hemisection with mirror-image drawing through the isthmal region in a racoon (*Procyon lotor*). Photomicrograph courtesy of Wally Welker.

small while the serotonin-containing raphe cells are extensive. In teleost fishes, the reverse is true. However, in amniotes, serotonin-containing cells are numerous in the raphe and also extensively invade more lateral areas of the tegmentum, and the locus coeruleus is also well developed and has numerous and widespread projections.

NUCLEUS ISTHMI

Group I

Nucleus isthmi is a group of cholinergic neurons that has reciprocal projections with the optic tectum. It is highly conserved across vertebrates; among Group I fishes, it has been identified in lampreys and nonteleost ray-finned fishes, including sturgeons and gars. In the latter, it lies on the lateral edge of the isthmal region (Fig. 16-2). Nucleus isthmi is a large and prominent nucleus in frogs, lying ventral to the caudal part of the optic tectum (Fig. 16-4). It is reciprocally and topographically connected with the optic tectum in both nonteleost ray-finned fishes and anuran amphibians. Recent results in frogs indicate that nucleus isthmi may play a role in enhancing the input to the tectum from retinal afferent fiber terminals by affecting their intake of calcium; this enhancement may thus promote the ability of the frog to orient and focus attention on a particular prey stimulus. In addition to its visual system connections, the nucleus isthmi also projects to the auditory

midbrain in frogs, the torus semicircularis, as well as to several tegmental and hindbrain nuclei related to the auditory system.

In the tegmentum of the coelacanth and lungfishes, a nucleus called the **superficial isthmal nucleus** has been identified (Fig. 16-3). However, this nucleus, unlike the nucleus isthmi of ray-finned fishes and amphibians, receives retinal projections and may thus be a different, unrelated cell group. Its other connections are unknown.

Group II

Whether a nucleus isthmi is present in hagfishes has not yet been determined. A nucleus that previously has been labeled nucleus isthmi in galeomorph sharks and skates does not meet the criteria for this nucleus in other vertebrates. In sharks, it does not project to the optic tectum, and it lacks cholinergic neurons. Nucleus isthmi is present in teleosts, with a distinctive lamina of cells surrounding a relatively cell-free central neuropil. It is reciprocally and topographically connected with the optic tectum. This nucleus is large in some species of teleosts, including eels and trout, but of more modest size in others. In addition to its tectal connections, it is also interconnected with the pretectum. In percomorph teleosts, such as the filefish *Navodon*, the nucleus isthmi receives an input from nucleus pretectalis, although this projection is lacking in other teleosts, such as carp. A projection

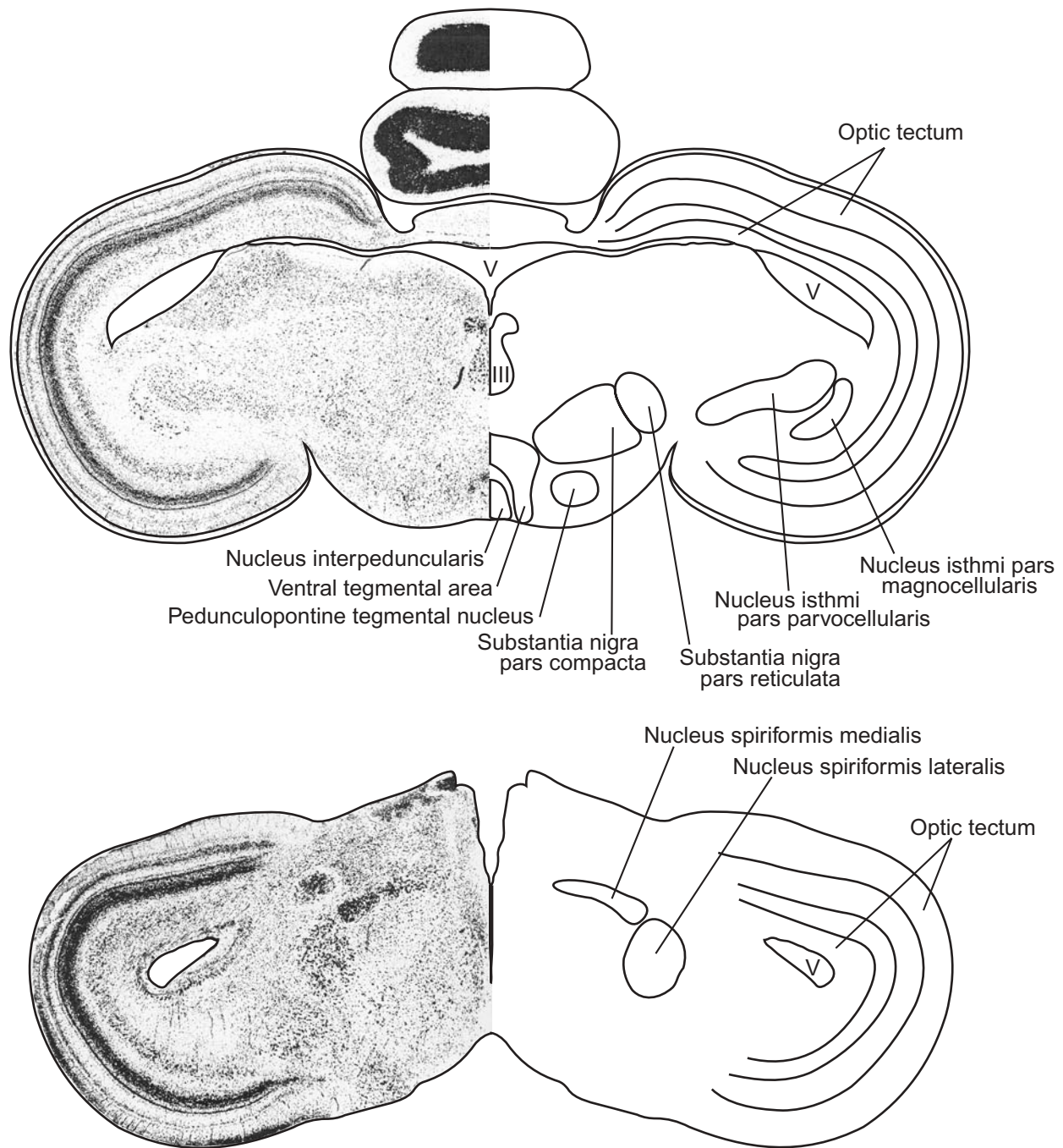


FIGURE 16-9. Transverse hemisections with mirror-image drawings through the isthmus and caudal tegmentum of the pigeon (*Columba livia*). The more caudal section is at the top. Note that only two of the three isthmal nuclei are shown. Adapted from Karten and Hodos (1967). Used with permission of The Johns Hopkins University Press.

from nucleus isthmi to nucleus pretectalis superficialis pars parvocellularis (PSP) may be a more general feature of teleosts.

Nucleus isthmi is called the **parabigeminal nucleus** in mammals and lies rostrally, at the level of the tegmentum proper. Parabigeminal roughly translates to “beside the two sets of twins,” the two sets of twins being the two paired sets of the inferior and superior colliculi (= the torus semicircularis and

optic tectum, respectively). The nucleus is reciprocally and topographically connected with the optic tectum in amniotes, as it is in fishes and amphibians. In mammals, the parabigeminal nucleus has also been found to project to two dorsal thalamic visual nuclei—to part of the lateralis posterior/pulvinar complex, which also receives a major direct input from the superior colliculus, and to the dorsal lateral geniculate nucleus,

which receives substantial direct retinal projections. In the latter nucleus, parabigeminal projections overlap another set of afferent projections to it from the superior colliculus.

Electrophysiological studies in mammals have found that the responses of parabigeminal cells to light stimuli are very like the responses of tectal cells. The tectal and parabigeminal cells are most responsive to a point of light moving in a specific direction, that is, they are "direction selective." They do not selectively respond to the size or the speed of the light stimulus. The parabigeminal nucleus has been characterized as a "satellite" system for the optic tectum, used to monitor and modulate the responses of the tectal cells. Given the properties of the isthmal/parabigeminal cells, one can surmise that this nucleus helps the optic tectum help a frog to catch a fly by adjusting for the directional component of the fly's movement. It would in like manner assist the optic tectum of fishes and amniotes in capturing moving prey.

In reptiles (see Fig. 15-5), nucleus isthmi lies in a dorso-lateral position in the isthmal region. It has reciprocal connections with the optic tectum, and it also projects to the directly tectorecipient nucleus rotundus in the dorsal thalamus. As in anamniotes, nucleus isthmi contains cholinergic neurons in reptiles, birds and mammals, and these neurons provide both inhibitory and excitatory inputs to the tectum and thalamus. In turtles, two divisions have been recognized—**nucleus isthmi pars magnocellularis** (Ipm) and **nucleus isthmi pars parvocellularis** (Ipc). Three nuclei are present in the isthmal region in birds (see Fig. 15-6)—**nucleus isthmi pars parvocellularis** (Ipc), **nucleus isthmi pars magnocellularis** (Ipm), and **nucleus isthmi pars semilunaris** (SLu). All three of these nuclei receive tectal projections. The Ipc/SLu nuclei project back to the optic tectum in a precise topographic arrangement, while the projections of Ipm to the tectum are diffuse in their organization. Only Ipc and SLu contain cholinergic neurons; the neurons of Ipm appear to be GABAergic. The three isthmal nuclei in birds may play differing roles in influencing the visual receptive field properties of tectal neurons. The nuclei also differ in the extent of their connections. While the pars magnocellularis and parvocellularis confine themselves to a reciprocal tectal connection, the pars semilunaris has more extensive connections and appears to represent a separately differentiated part of the isthmal complex. It uniquely projects additionally to nucleus rotundus in the dorsal thalamus and to another nucleus as well, the lateral spiriform nucleus, which relays basal ganglia output into the deeper part of the tectum, affecting tectal motor outputs. The avian Ipm nucleus appears homologous to the Ipm of turtles. The Ipc/SLu isthmal nuclei of birds appear to be homologous to the Ipc division of turtles and to the parabigeminal nuclei of mammals.

Evolutionary Perspective

A nucleus isthmi that contains cholinergic neurons, is reciprocally and topographically connected with the optic tectum, and does not receive a direct retinal input appears to be present in all of the lampreys, cartilaginous fishes, ray-finned fishes, amphibians, and amniote vertebrates studied to date. Nucleus isthmi was thus probably present in the common ancestral stock of at least lampreys and all jawed vertebrates.

A cholinergic cell group in the isthmus that meets the connectional criteria for nucleus isthmi may well be present in the coelacanth and in lungfishes, but it remains to be studied in these taxa. If it is absent, it would presumably have been secondarily lost as a result of the general process of reduction of the brain within these taxa. The lack of migration of most cell groups throughout the brain in the coelacanth, lungfishes, and urodele amphibians appears to be the result of a trend to secondary simplification related to neoteny (the retention of embryonic characteristics in the adult). These groups of vertebrates are in fact excellent examples of the principal that brain evolution is multidirectional; there is not a single trend from simple to complex, as complex can also give rise to simple. Phylogenetic analysis of such simplified and reduced structures is particularly difficult, however, as many features of the morphology of the ancestral adult phenotype have been lost.

In amniotes, nucleus isthmi has projections to the dorsal thalamus in addition to its reciprocal connections with the optic tectum. Whether similar projections are present in any anamniotes remains to be investigated, but the isthmothalamic projections are at least shared among mammals, reptiles, and birds. In birds, a parcellation (see Chapter 6) of the isthmal region has occurred such that the isthmothalamic projections arise only from its semilunaris subdivision. Also, the magnocellular division contains GABAergic neurons in contrast to the cholinergic populations present in the other two divisions of this nucleus.

ISTHMO-OPTIC NUCLEUS

Group I

An isthmo-optic nucleus, that is, a group of neurons located in the caudal mesencephalon that project to the retina, has been found in a fragmented distribution both among and within various vertebrate groups. Tegmental retinopetal projections have been found in lampreys and in two nonteleost ray-finned fishes, bichirs and gars but are absent in another nonteleost ray-finned fish, sturgeons. Similar projections also appear to be absent in Group I sharks as well as in amphibians.

Group II

Isthmo-optic neurons that project to the retina have been found in hagfishes in the medial, rostral part of the mesencephalic tegmentum. The nucleus in hagfishes that contains the majority of the retinopetal cells is called the **nucleus of the posterior commissure** (rostral to the level shown in Fig. 16-5; see Fig. 20-5); additional retinopetal cells lie scattered in an area lateral to this nucleus. An isthmo-optic nucleus has not been found in any Group II cartilaginous fish. Isthmo-optic neurons have been found in one teleost, a pike, but are absent in other teleosts studied.

Among amniotes, isthmo-optic neurons have been found in crocodiles and turtles. Only a few such neurons are present in lizards, and no retinopetally projecting neurons are present in the tegmentum of snakes. In birds, an isthmo-optic nucleus is present in the dorsal, medial part of the tegmentum; this nucleus is cytoarchitectonically well defined in some species,

such as in the pigeon (see Fig. 15-6). A smaller number of retinopetal neurons also lie scattered in an area ventral to the isthmo-optic nucleus. The avian isthmo-optic nucleus is particularly well developed in birds that feed by pecking, such as pigeons, as opposed to those that feed on-the-wing, such as swifts and swallows.

Evolutionary Perspective

Retinopetally projecting isthmo-optic neurons are present in lampreys, hagfishes, some but not all nonteleost ray-finned fishes, at least one teleost, and, among amniotes, in some reptiles and in birds. Such neurons appear to be absent in all cartilaginous fishes, at least one nonteleost ray-finned fish (sturgeons), most teleosts, amphibians, snakes, and mammals. From this distribution, the evolutionary history of isthmo-optic neurons cannot be clearly discerned, particularly among jawed vertebrates.

Because they are present in both hagfishes and lampreys, isthmo-optic neurons were probably present in the earliest vertebrates and thus plesiomorphic for vertebrates. This population of neurons may have been lost in the common ancestral stock of jawed vertebrates, however, and subsequently regained independently within two groups of vertebrates—in some of the ray-finned fishes and in nonmammalian amniotes. Among the latter, because isthmo-optic neurons are present in lizards, crocodiles, and birds, their absence in snakes appears to be an apomorphy. Another possibility, that isthmo-optic neurons were retained in ancestral jawed vertebrates and subsequently lost multiple times, cannot be entirely ruled out, however. Thus, whether the isthmo-optic neurons present in nonmammalian amniotes are historically homologous or homoplasious to those in some ray-finned fishes cannot be determined from the present data. Also, whether their generative bases are the same and inherited from a common ancestor—i.e., whether the various isthmo-optic neuronal populations are generatively homologous—also remains to be determined.

MIDBRAIN LOCOMOTOR REGION AND PEDUNCULOPONTINE TEGMENTAL NUCLEUS

Group I

In the isthmal region of most vertebrates, multiple groups of cholinergic neurons are present, including nucleus isthmi and the Edinger-Westphal and somatic motor components of the oculomotor nuclear complex (see Chapter 12). Two of these cholinergic cell groups are present at about the level of the trochlear nucleus, which is itself cholinergic—the **laterodorsal tegmental nucleus** and the **pedunculopontine tegmental nucleus**. The latter is the main component of the **midbrain locomotor region (MLR)**, which appears to be a **command generator** for sequences of movements. Stimulation of the MLR (Fig. 16-1) produces locomotory movements, presumed to be mediated by projections to the reticular formation, and hence to the spinal cord. In lampreys, a cholinergic cell group is present at the level of the trochlear nucleus

within the tegmental region that borders the ventricle. Stimulation of these cells produces locomotor activity, indicating that they comprise an MLR that presumably sends descending projections to the reticular formation. They appear to be homologous to the pedunculopontine tegmental nucleus (and perhaps also to the laterodorsal tegmental nucleus) of other vertebrates. Several small groups of cholinergic neurons are also present within the isthmal reticular formation in sturgeons, some of which may likewise be historically homologous to the pedunculopontine tegmental nucleus of other vertebrate groups.

Group II

In stingrays, a midbrain locomotor region has been found that includes the interstitial nucleus of the medial longitudinal fasciculus and the medial part of a cell group called the **cuneiform nucleus** (Fig. 16-6). Stimulation of this region evokes locomotory movements in the pectoral fin. The region projects bilaterally to the magnocellular/gigantocellular region of the medullary reticular formation, which in turn projects to the spinal cord. The MLR in cartilaginous fishes appears to correspond to the lateral subdivision of a similarly located MLR in mammals. Very few cholinergic neurons are present in the isthmal region in sharks, so a pedunculopontine tegmental nucleus has not been identified in this group. Another nucleus in this region is the **intercollicular nucleus**. It lies near the cuneiform nucleus in a transition zone between the optic tectum and the torus semicircularis. In skates, this nucleus receives projections from the optic tectum and projects to the spinal cord, forming a tectal motor relay pathway complementary to the tectoreticular pathway.

In teleost fishes, a midbrain locomotor region has been identified in the dorsocaudal tegmentum near the midline, a position similar to that of the MLR in stingrays. Weak stimulation of the area produces movements of the pectoral fins, while stronger stimulation produces movement of both the pectoral and caudal fins. Further, a group of cholinergic neurons that lies lateral to nucleus isthmi and is referred to as the dorsolateral tegmental nucleus in trout is a good candidate for a homologue of the pedunculopontine nucleus based on its histochemistry and position.

Among amniotes, the midbrain locomotor region has been studied primarily in mammals. The MLR includes the caudal part of the cuneiform nucleus and also involves another, neighboring nucleus, the pedunculopontine tegmental nucleus. The latter nucleus receives input from the deep cerebellar nuclei and projects rostrally to the substantia nigra pars compacta (see Chapter 17) and the subthalamic nucleus (see Chapter 24). It appears to serve as an interface between the cerebellum and striatopallidal circuits. The MLR also gives rise to descending projections, mainly from the **cuneiform nucleus**, to the reticular formation via the medial longitudinal fasciculus. Stimulation of the MLR produces walking movements. In fact, this region takes its name from the observation (first made in anesthetized cats) that stimulation of it results in rhythmic patterns of limb movements similar to those used by the waking animal when walking.

In birds, a locomotor region has been found in the region of a nucleus called the **lateral spiriform nucleus** (Fig. 16-9). Stimulation in this region produces walking and wing flapping

motions. The lateral spiriform nucleus receives its major inputs from the globus pallidus, subthalamic nucleus, and substantia nigra. Its sole efferent projection is to the deeper layers of the optic tectum [layers 8–13, with the heaviest projection being to layers 11–13 (see Chapter 18)]. It thus serves as a relay between the basal ganglia and the deeper layers of the tectum, which themselves give rise to descending projections to hind-brain motor-related cell groups. A **pedunculopontine tegmental nucleus** is also present in birds (Fig. 16-9), as it is likewise in reptiles. This nucleus is a collection of cholinergic neurons that lies in the ventromedial part of the midbrain tegmentum. Its connections are similar to the nucleus of the same name in mammals.

Evolutionary Perspective

A midbrain locomotor region, which in jawed vertebrates produces coordinated, purposeful movements of the fins, limbs, or wings (i.e., the appendicular skeleton) when stimulated, has been identified in a wide variety of extant vertebrates. It has been found in both lampreys and hagfishes, cartilaginous fishes, teleost fishes, and in mammals and birds. An MLR was thus apparently present in the common ancestral stock of all vertebrates and represents a very old system for the production of locomotory motor behaviors.

INTERPEDUNCULAR NUCLEUS

Group I

An interpeduncular nucleus has recently been identified in the ventral part of the mesencephalon in lampreys (Fig. 16-1), based on a major afferent input from the habenula via the fasciculus retroflexus. The interpeduncular nucleus in squalomorph sharks lies medial to the rostral part of the reticular formation and immediately rostral to the raphe and caudal to the ventral tegmental area. The fasciculus retroflexus traverses the medial tegmental region to project to the interpeduncular nucleus. In nonteleost ray-finned fishes, the interpeduncular nucleus (Fig. 16-2) and fasciculus retroflexus lie in similar positions, respectively. The interpeduncular nucleus is rather small and cell sparse in these fishes. In frogs, the interpeduncular nucleus is well developed and lies in the isthmus (Fig. 16-4).

Group II

In hagfishes, a large interpeduncular nucleus and a correspondingly large habenula are present, but the interpeduncular nucleus lies farther rostrally than in most animals. In these fishes, it lies in a ventromedial position at levels through the diencephalon rather than in the isthmus or caudal tegmentum. The position of the fasciculus retroflexus has not been established.

The interpeduncular nucleus is larger and more distinct in cartilaginous fishes with elaborated brains than in squalomorph sharks. It lies in a medial position in the ventral tegmentum and receives projections via the fasciculus retroflexus. In teleosts (Fig. 16-7) and amniotes (Fig. 16-9), the interpeduncular nucleus lies in the ventromedial part of the tegmentum, and

the fasciculus retroflexus projects to it from the habenula. In mammals, the pes pedunculi lies ventrolateral to the nucleus.

Evolutionary Perspective

The fasciculus retroflexus, the habenula in the diencephalon from which it arises, and the interpeduncular nucleus to which it projects are common features of vertebrates and are assumed to have been present in the ancestral stock of all vertebrates. This system is the route by which input from striatal and limbic related areas of the telencephalon reaches the tegmentum and can be integrated there with other incoming sensory information for coordination with the appropriate motor responses.

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17

Tegmentum and Tori

INTRODUCTION

The main part of the midbrain tegmentum lies rostral to the isthmus and ventral to the tectum (or roof) of the midbrain. For designating the regions that lie ventral to the tectum in mammals, the terminology approaches bedlam. The word **tegmentum** is derived from the Latin *tegmen* and means cover. It is so named because in mammals it lies dorsal to and thus “covers” the **basis pedunculi**—a term applied to the substantia nigra and the set of major descending motor tracts (corticopontine, corticobulbar, and corticospinal) that lie on the ventral-most aspect of the midbrain. The set of tracts is most correctly referred to as the **pes pedunculi**, an odd Latin phrase that means “the foot of the little foot.” An alternate term, **crus cerebri**, is used either as a synonym of basis pedunculi or of pes pedunculi. The term **cerebral peduncle** is also used frequently as a synonym of pes pedunculi, but its more correct usage applies to the entire midbrain ventral to the tectum, i.e., the tegmentum and the basis pedunculi. Fortunately, in non-mammalian vertebrates, the term tegmentum is simply applied to all structures ventral to the tectum, including the substantia nigra, since a major set of descending tracts comparable to the pes pedunculi is not present on the ventral surface of the midbrain. This terminological muddle should not be given much attention, as most seasoned professionals rarely heed it, simply referring to three parts of the mammalian midbrain as tectum, tegmentum (including the substantia nigra), and the cerebral peduncle, with the latter term referring only to the corticopontine, corticobulbar, and corticospinal fiber tracts.

In addition to cranial nerve nuclei and ascending and descending tracts discussed earlier, some structures that are

considered here are involved in the production and control of various motor functions, such as the **mesencephalic nucleus of the trigeminal nerve** and the **red nucleus**. The **substantia nigra** also will be discussed here, as will its related, more medially lying, dopaminergic cell group, the **ventral tegmental area**. Two additional midbrain structures are also discussed in this chapter: the **torus lateralis**, of which little is known, and the **torus semicircularis**, which receives ascending auditory and lateral line projections via the lateral lemniscus. The torus lateralis and torus semicircularis are part of the roof of the midbrain, lying in a region between the optic tectum and the tegmentum. A third torus, called the **torus longitudinalis**, is discussed in conjunction with the cerebellum in Chapter 14 and with the optic tectum in Chapter 18. A number of the nuclei and fiber tracts in the tegmentum, with other structures labeled for orientation, are illustrated in some animals with laminar brains in Figures 17-1–17-6 and in other animals with elaborated brains in Figures 17-7–17-12 and 17-15–17-16.

MESENCEPHALIC NUCLEUS OF THE TRIGEMINAL NERVE

Group I

A mesencephalic nucleus of the trigeminal nerve (MesV) has not been found in lampreys. Both the trigeminal and facial nerves are known to be involved in producing movements of the sucking apparatus of the mouth, so it is possible that a MesV might be present in these fishes. In squalomorph sharks, as in other jawed vertebrates, MesV cells are present and

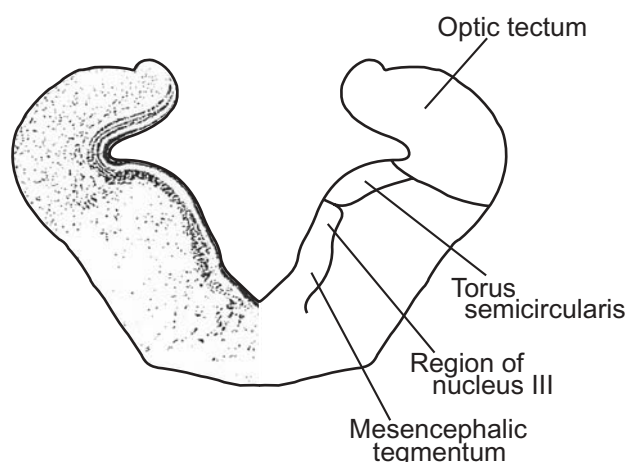


FIGURE 17-1. Transverse hemisection with mirror-image drawing through the tegmentum of a lamprey (*Petromyzon marinus*). Adapted from Kennedy and Rubinson (1977) and used with permission of John Wiley & Sons. Note that in this and in subsequent figures, ventricles are generally not labeled.

receive proprioceptive feedback from the muscles of the jaws. The nucleus lies in the medial part of the periventricular gray layer of the optic tectum (Fig. 17-2) in these sharks, and it lies in a similar position in nonteleost ray-finned fishes and in amphibians. Although they lie within the tectum, the MesV cells are neural crest-derived trigeminal cells and are thus discussed in this chapter.

Group II

In hagfishes, as in lampreys, a MesV has not been identified. In cartilaginous fishes with elaborated brains (Fig. 17-8) and teleost fishes, cells of MesV are present dorsally in the periventricular gray of the optic tectum. MesV is unusually large in some teleosts [see Fig. 11-2(D)]. The cells of MesV lie in the periventricular gray of the tectum in mammals (Fig. 17-12), reptiles (Fig. 17-15), and birds. In many mammals, the cells are present throughout the rostrocaudal extent of the midbrain roof (Figs. 16-8 and 17-12).

Evolutionary Perspective

The mesencephalic nucleus of V is a very constant feature of the brain in all jawed vertebrates and thus is thought to have been present in the common ancestral stock of this large group. Whether cells are present in lampreys and hagfishes that are homologous to the MesV cells in jawed vertebrates remains to be determined.

RED NUCLEUS AND RELATED NUCLEI

Group I

A red nucleus does not appear to be present in lampreys. In squalomorph sharks, a red nucleus is present in the ventral part of the tegmentum (Fig. 17-2) and receives projections from

the cerebellar nuclei via the brachium conjunctivum. However, unlike the case in most other animals, the red nucleus does not appear to project to the spinal cord. A second nucleus related to the cerebellum, named **nucleus H**, is present at a more rostral level (Fig. 17-2).

Among nonteleost ray-finned fishes, a red nucleus has been identified in gars in the rostral tegmentum (Fig. 17-3) on the basis of projections to the spinal cord via the **rubrospinal tract**. In lungfishes, a red nucleus has similarly been identified on the basis of its giving rise to descending projections to the spinal cord (Fig. 17-5). A red nucleus is also present in amphibians. In frogs, it lies in the ventral part of the tegmentum (Fig. 17-6), projects to the contralateral spinal cord, and receives a sparse, descending projection from the striatum in the basal telencephalon. It has also been found to project to the cerebellar hemisphere and to receive projections from the deep cerebellar nucleus.

Group II

Hagfishes are similar to lampreys in that they appear to lack a red nucleus. Cartilaginous fishes with elaborated brains have a relatively large red nucleus, bordered by the brachium conjunctivum. The nucleus lies in the ventral tegmentum (Figs. 17-8 and 17-9) at the level of the oculomotor nucleus, and it projects to the spinal cord. Scattered cells, which correspond to the nucleus H present in squalomorph sharks, lie in the lateral part of the tegmentum (Fig. 17-8). This nucleus is reciprocally connected with the cerebellum. More rostrally, an additional migrated nucleus, called **nucleus K** (Fig. 17-9), is present and is also believed to be connected with the cerebellum. Like the red nucleus, nuclei H and K are devoid of catecholamine-containing cells.

In teleosts, the brachium conjunctivum (Fig. 17-10) runs rostroventrally through the tegmentum and decussates just dorsal to the interpeduncular nucleus. It projects to the red nucleus, a small, discrete group of cells (Fig. 17-10). The position of the teleost red nucleus is more dorsal and more medial than in cartilaginous fishes, and its cells appear larger and more tightly condensed.

In both mammals (Fig. 17-12) and birds (Fig. 17-16), the red nucleus is a rather large and prominent tegmental nucleus. The connections of the red nucleus have been found to be very similar in these two groups of amniotes. In both groups, the afferent projections to the red nucleus arise in a somatomotor part of the pallium in the telencephalon and in cerebellar nuclei. The major efferent projection of the nucleus is to the contralateral spinal cord, via the rubrospinal tract.

In most reptiles, the red nucleus lies in the ventrolateral part of the rostral tegmentum (Fig. 17-15). Descending projections from the striatum terminate just rostral to it in the **pre-rubral area**. The red nucleus gives rise to a rubrospinal tract that projects to the contralateral spinal cord. A rubrospinal tract is absent in pythons, but this absence cannot be correlated with the absence of limbs, since the tract is present in colubrid snakes.

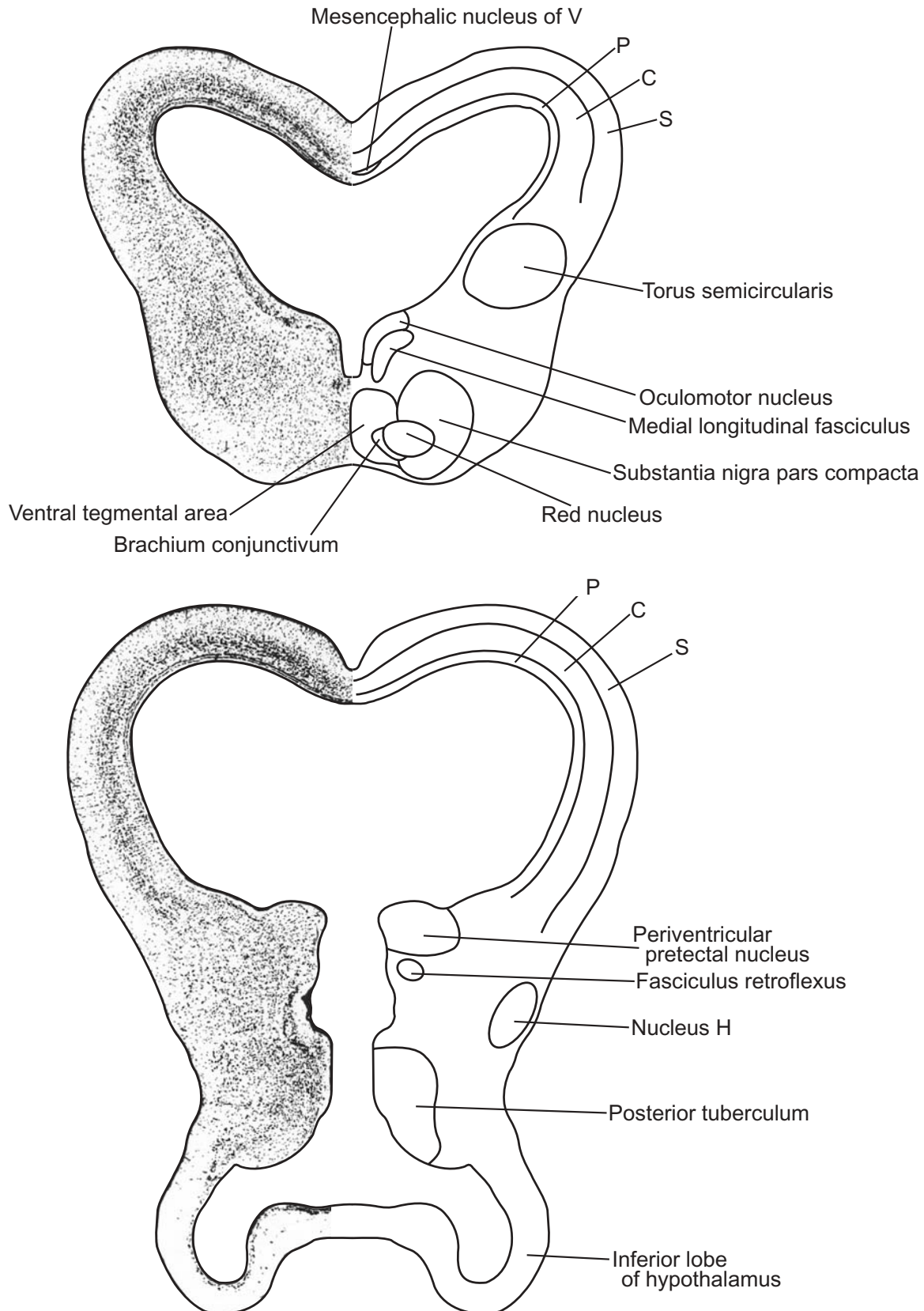


FIGURE 17-2. Transverse hemisections with mirror-image drawings through the tegmentum of a squalomorph shark (*Squalus acanthias*). The more caudal section is at the top. Adapted from Northcutt et al. (1988) and used with permission of John Wiley & Sons. In this and some subsequent figures, S, C, and P indicate the superficial, central, and periventricular zones of the optic tectum.

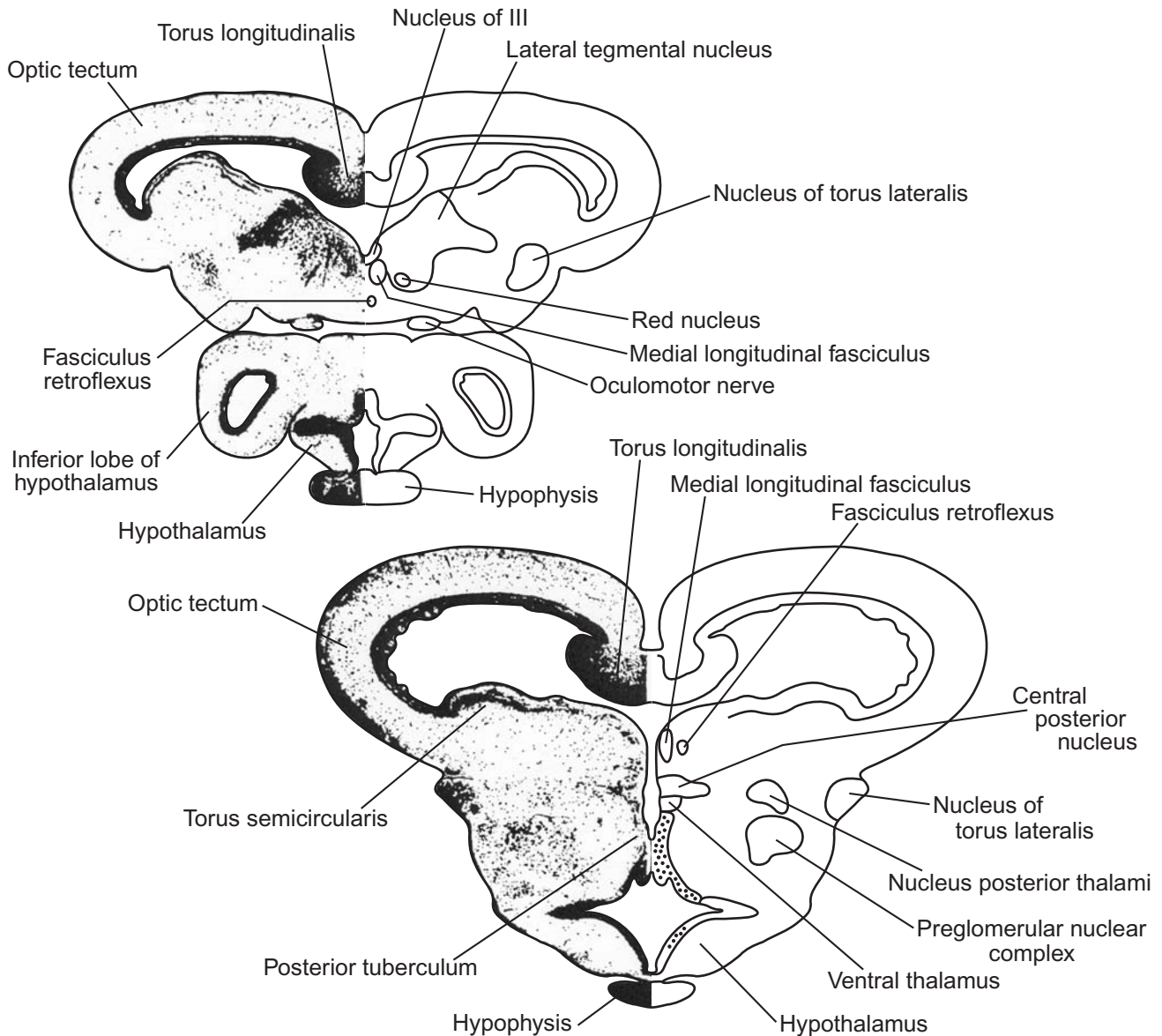


FIGURE 17-3. Transverse hemisections with mirror-image drawings through the tegmentum of a longnose gar (*Lepisosteus osseus*). The more caudal section is at the top. Adapted from Northcutt and Butler (1980) with additional data from Northcutt (1983). Used with permission of Elsevier.

Evolutionary Perspective

A red nucleus is absent in agnathans, and its absence may be correlated with the limited development of the cerebellum in these animals. A red nucleus is present in cartilaginous fishes, ray-finned fishes, lungfishes, amphibians, and amniotes and is thus plesiomorphic for jawed vertebrates. Descending projections to the contralateral spinal cord from this nucleus are also widely distributed among jawed vertebrates but have not been found in a squalomorph shark and, among reptiles, are absent in pythons but present in colubrid snakes. The rubrospinal tract is thought to be primarily involved with movements of the limbs. This system is quite conservative, however; its organization is very similar in birds and mammals, for example,

despite differences in the particular movements of the limbs. The rubrospinal system may have additional functions as well, as it is present in a least one snake and in both South American and African lungfishes, only the latter of which can use their fins for assistance in movements.

SUBSTANTIA NIGRA AND VENTRAL TEGMENTAL AREA

In amniotes and possibly anamniotes as well, the substantia nigra consists of two divisions—a pars compacta and a pars reticulata. The latter contains GABAergic neurons that have

widespread projections. The substantia nigra pars compacta and ventral tegmental area, where present, are characterized by the presence of catecholamine-containing cells; they project heavily upon the striatal region in the telencephalon and are part of a functional system for the initiation and regulation of movement. Other catecholamine-containing cell groups also occur in the brainstem, however, and we need to clarify the

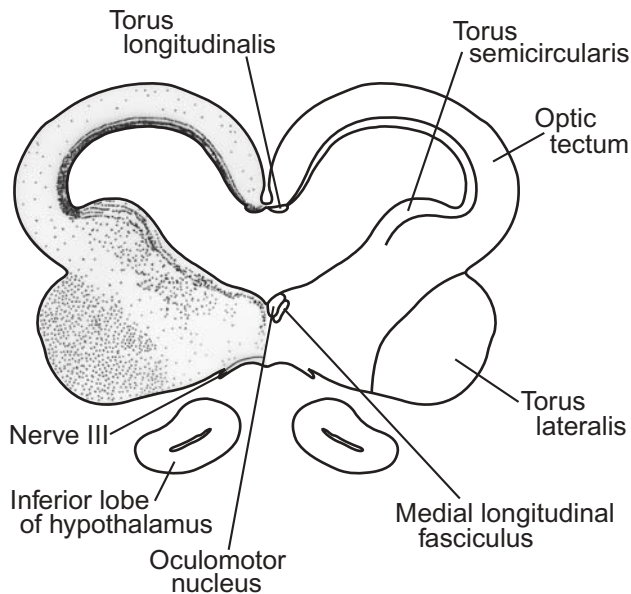


FIGURE 17-4. Drawing of a transverse hemisection with mirror-image outline drawing through the tegmentum of a bowfin (*Amia calva*). Adapted from Nieuwenhuys and Pouwels (1983) and used with permission of the University of Michigan Press.

nomenclature and anatomy of these groups (see also the discussion in Chapter 13, including Fig. 13-14).

In 1964, A. Dahlström and K. Fuxe proposed a system of nomenclature for the catecholamine-containing cell groups in the brains of mammals; this system is now widely accepted and also applied to nonmammalian vertebrates where possible. They recognized 12 groups of such cells and labeled them **A1** to **A12** in their caudal-to-rostral sequence. At least 17 such cell groups are now recognized. In this system, some catecholamine-containing cells caudal to the red nucleus, in the **retrobulbar area**, form the **A8** cell group. The substantia nigra pars compacta is the **A9** cell group, and the ventral tegmental area is the **A10** cell group. The catecholamine of the A8-A10 neuronal cell groups is the neurotransmitter dopamine.

In many anamniote vertebrates, dopamine-containing cells also occur in a nucleus in the caudal part of the diencephalon called the **posterior tuberculum** (see Chapter 20). The posterior tuberculum lies just rostral to the area of the tegmentum, which contains the ventral tegmental area and the substantia nigra in some anamniote vertebrates. Recent developmental studies indicate that the dopaminergic neuron population of the posterior tuberculum of anamniotes is most likely homologous to the A8/A9/A10 groups in amniotes and possibly to the caudal diencephalic (A11) dopaminergic neuron group as well.

Group I

Some cells within the mesencephalic tegmentum of lampreys (Fig. 17-1) contain dopamine. These cells are located in the more rostral and ventral part of this region and may correspond to cells in the posterior tuberculum of other vertebrates. Among cartilaginous fishes, dopamine-containing cells are present in the posterior tuberculum of ratfishes (chimaeras) but not more caudally within the mesencephalon. In squalo-

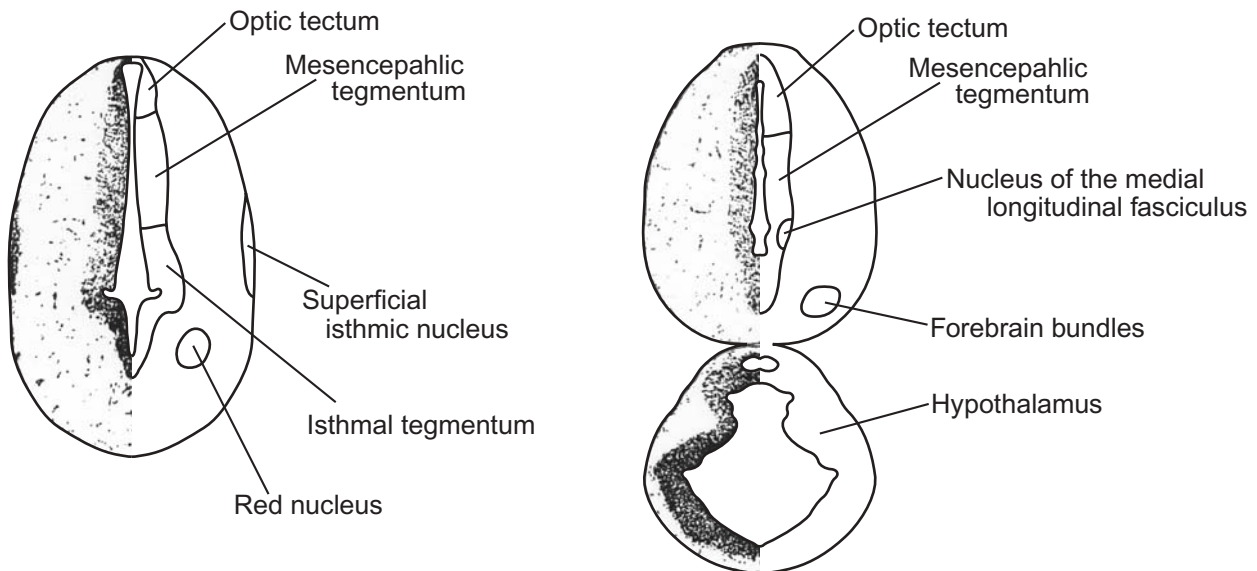


FIGURE 17-5. Drawing of a transverse hemisection with a mirror-image drawing through the tegmentum of a lungfish (*Protopterus annectens*). The more caudal section is on the left. Adapted from Northcutt (1977) and used with permission of John Wiley & Sons.

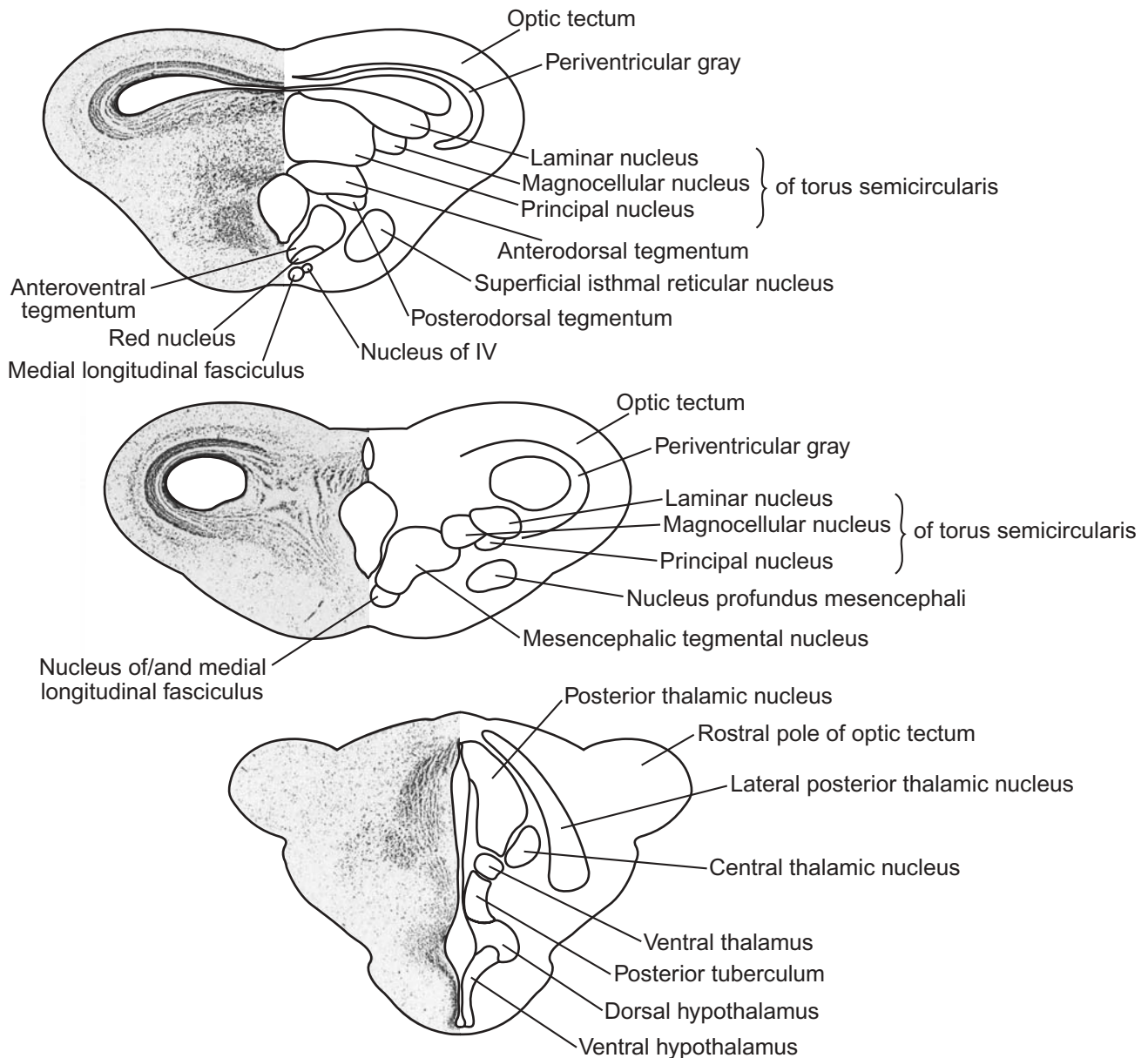


FIGURE 17-6. Drawings of transverse hemisections with mirror-image drawings through the tegmentum of a frog (*Rana catesbeiana*). The most caudal drawing is at the top. Adapted from Wilczynski and Northcutt (1983) and integrated with additional data from Feng and Lin (1991) on *Rana pipiens*. Used with permission of John Wiley & Sons.

morph sharks, however, there are dopamine-containing cells in the posterior tuberculum and also more caudally in an area surrounding the red nucleus. The medial part of this latter area thus can be recognized as the ventral tegmental area because of its position rostral to the interpeduncular nucleus and medial to the red nucleus and because it has dopamine-containing cells (Fig. 17-2). The dopamine-containing cells that lie around the lateral edge of the red nucleus appear to constitute the substantia nigra.

In nonteleost ray-finned fishes, separate nuclei forming a ventral tegmental area and substantia nigra are absent. Dopamine-containing cells (represented by the large dots in

Fig. 17-3) are for the most part confined to the posterior tuberculum of the diencephalon. A posterior tuberculum has been identified in both lungfishes and amphibians (Fig. 17-6), and, as in teleosts, the only dopamine-containing cells in the rostral part of the brainstem in amphibians are a small number within the posterior tuberculum. In frogs, some of the cells in the posterior tuberculum have been found to project to the striatum.

Group II

In the mesencephalic tegmentum of hagfishes (Fig. 17-7), **dorsal and ventral tegmental nuclei** have been identified,

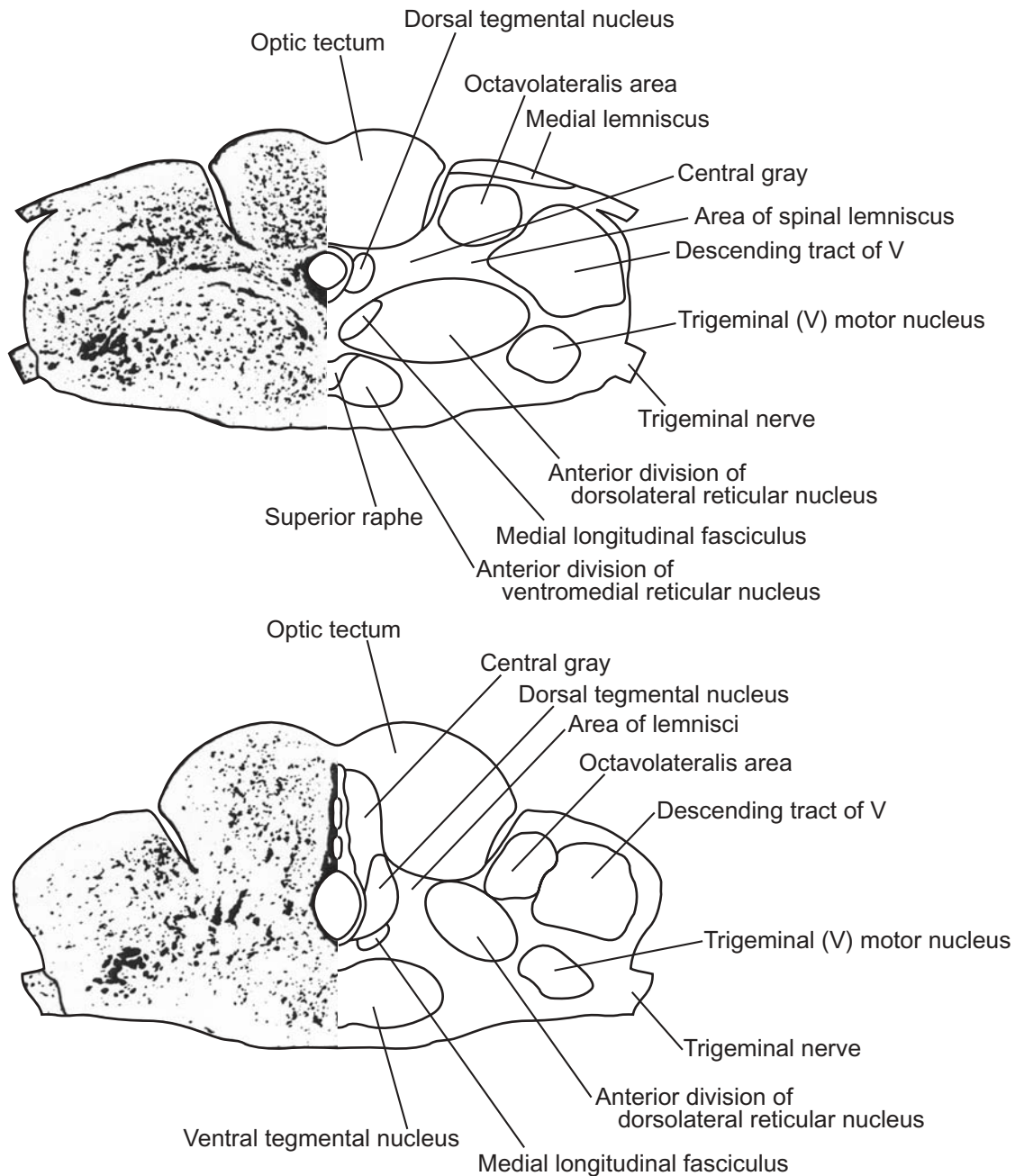


FIGURE 17-7. Drawings of transverse hemisections with mirror-image drawings through the tegmentum of a hagfish (*Eptatretus stouti*). The more caudal section is at the top. Adapted from Ronan and Northcutt (1990) and used with permission of John Wiley & Sons.

which lie dorsal and ventral to the medial longitudinal fasciculus, respectively. The ventral tegmental nucleus is particularly large and extends rostrally. Unfortunately, we do not yet know whether any catecholamine-containing cells are present in this region, although the area tentatively identified as striatum in the telencephalon does receive a dopaminergic input.

Both the ventral tegmental area and substantia nigra are present and relatively large in galeomorph sharks, skates, and rays. In Figure 17-9 we show four levels in between the two

sections shown in Figure 17-8 for more detail of the nuclei within the ventral part of the tegmentum. The dots in Figure 17-9 represent catecholamine-containing cells. The most rostral level in Figure 17-9 is through the posterior tuberculum, which also has numerous catecholamine-containing cells.

There are no migrated nuclei corresponding to the ventral tegmental area or substantia nigra in teleosts. Dopamine-containing cells in this region are confined to the posterior tuberculum (Fig. 17-10), as in nonteleost ray-finned fishes and

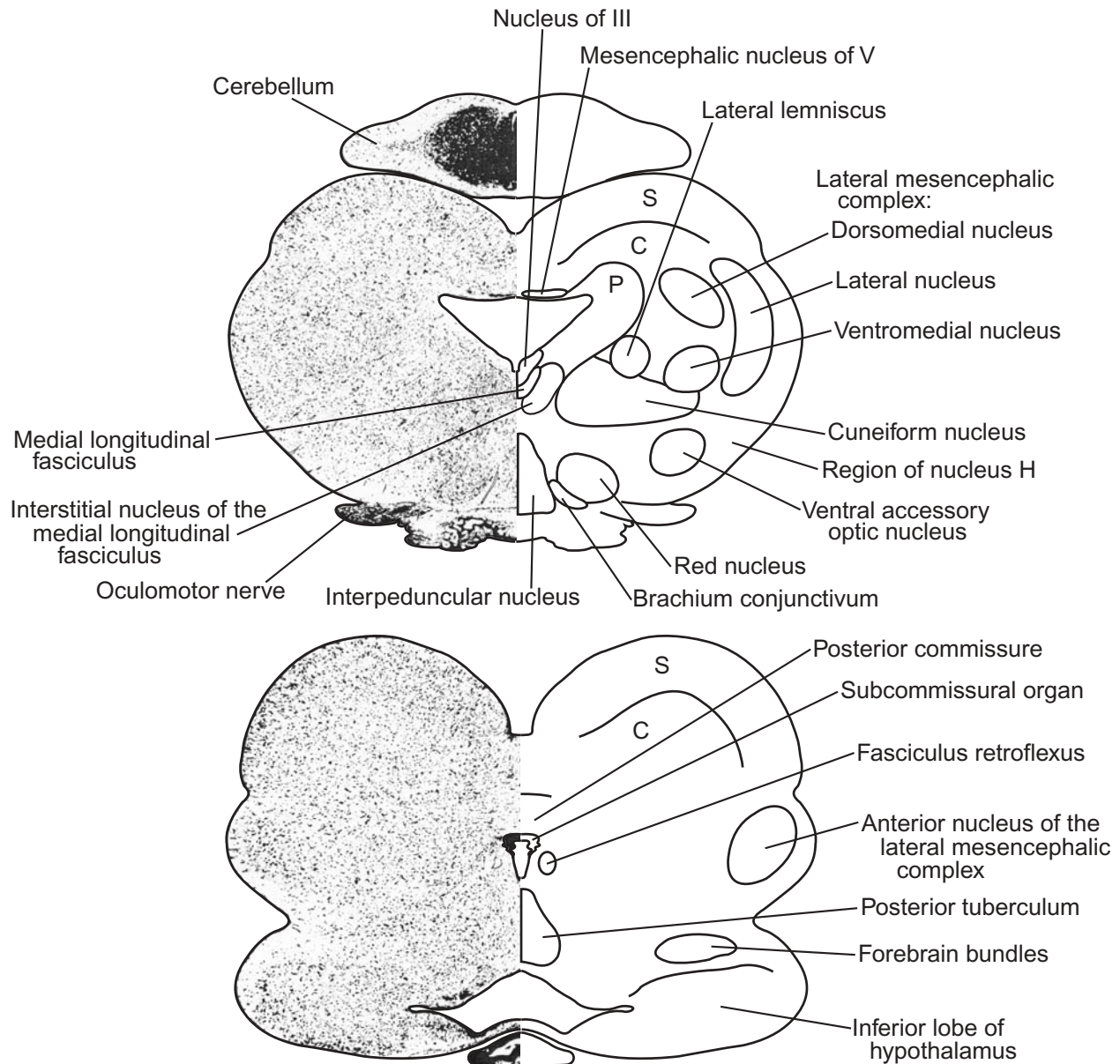


FIGURE 17-8. Transverse hemisections with mirror-image drawings through the tegmentum of a skate (*Raja eglanteria*). The more caudal section is at the top. Adapted from Boord and Northcutt (1982) and used with permission of John Wiley & Sons.

in contrast to sharks, skates, and rays. These dopaminergic neurons appear to represent the homologous cell population of the substantia nigra/ventral tegmental area of amniotes.

In amniotes, a great deal has been learned about the connections of the substantia nigra and the ventral tegmental area. The neurotransmitters of the various projections have also been identified in many cases. These nuclei and their connections, particularly those with the striatum, have received so much attention because of the involvement of the substantia nigra in diseases of humans that are characterized by abnormal, involuntary movements, such as Huntington's (chorea) and Parkinson's (paralysis agitans) diseases. The substantia nigra and ventral tegmental area are involved in the initiation and regulation of movements. We will discuss this system in more depth

than many of the other systems because it can serve to some extent as a model of the complexity and interactions that occur in most systems but are worked out in detail in so few.

A region corresponding to the posterior tuberculum of anamniotes has not been found in amniotes, but dopamine-containing cells are present in part of the substantia nigra pars compacta and in the ventral tegmental area (Figs. 17-12, 17-15, and 17-16). Although the specific arrangement of the neuron populations of the substantia nigra differ somewhat among amniotes, and the "compacta" and "reticulata" adjectives apply best to mammals, these designations are used for consistency in birds (see Table 15-1) and reptiles as well.

The pars reticulata lacks dopamine-containing cells and instead contains inhibitory, GABAergic neurons. It is the area

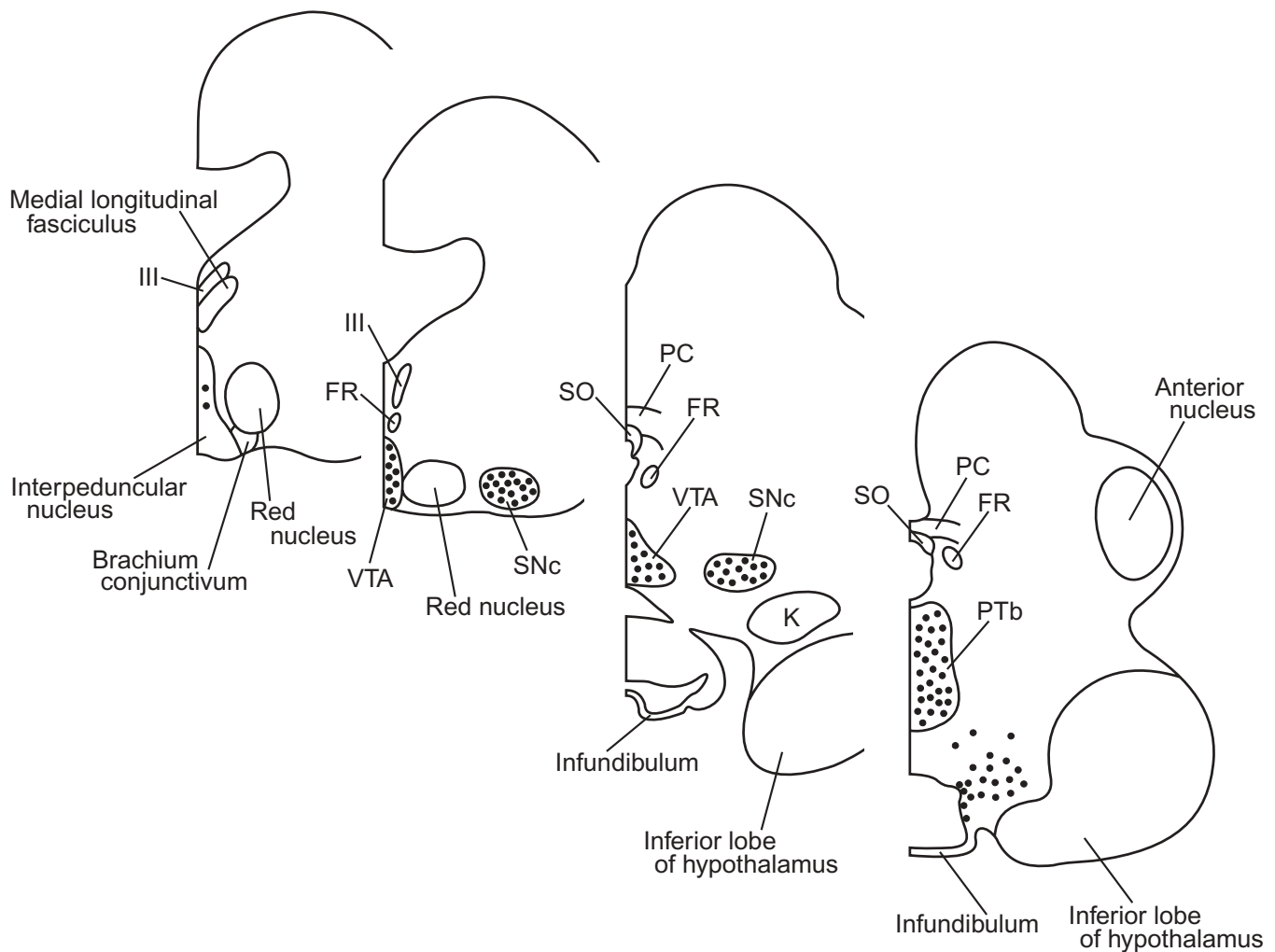


FIGURE 17-9. Drawings of caudal-to-rostral (as left to right) transverse hemisections through the tegmentum of a skate (*Raja radiata*) to show the positions of the substantia nigra, red nucleus, and ventral tegmental area. The most caudal and rostral levels are approximately the same as those shown in the caudal and rostral levels of *Raja eglanteria* in Figure 17-8, respectively. Dopamine immunoreactive cell bodies are indicated by dots. Adapted from Meredith and Smeets (1987) and used with permission of John Wiley & Sons.

where a number of afferent projections terminate, and it gives rise to widespread efferent projections. The cells in the pars compacta of the substantia nigra and the ventral tegmental area project heavily to the striatum in the telencephalon. The loss of the cells that produce dopamine in the substantia nigra is the basis for Parkinson's disease.

The striatum, or **striatopallidal complexes** (see Chapters 19 and 24), in the ventrolateral part of the telencephalon consists of a number of parts. We need to digress momentarily to list them here, since many of them are interconnected with the substantia nigra and ventral tegmental area. The dorsal striatopallidal complex contains the **dorsal striatum** and **dorsal pallidum**, and the ventral striatopallidal complex contains the **ventral striatum** and **ventral pallidum** (see Table 19-1). The dorsal striatum is composed of two structures called the caudate nucleus and the putamen, and the dorsal pallidum is a nucleus called the globus pallidus. In mammals but not in other

amniotes, the globus pallidus has two parts, external and internal. The major components of the ventral striatum are nucleus accumbens and the olfactory tubercle, whereas the ventral pallidum consists of a population of scattered neurons in an area called the substantia innominata. The components of the striatopallidal complexes are related not only to the motor system but to the limbic parts of the telencephalon (that function in learning and emotion) as well. The connections of the striatopallidal complexes with the groups of dopamine-containing neurons in the midbrain also encompass both the motor- and limbic-related forebrain systems.

Some of the connections of the substantia nigra pars compacta are shown in Figure 17-13. Its main output is to the caudate-putamen with which it is reciprocally connected, as is also the case with nucleus accumbens, the external part of the globus pallidus, and the substantia nigra pars reticulata. It also receives inputs from neocortex and from the pedunculopon-

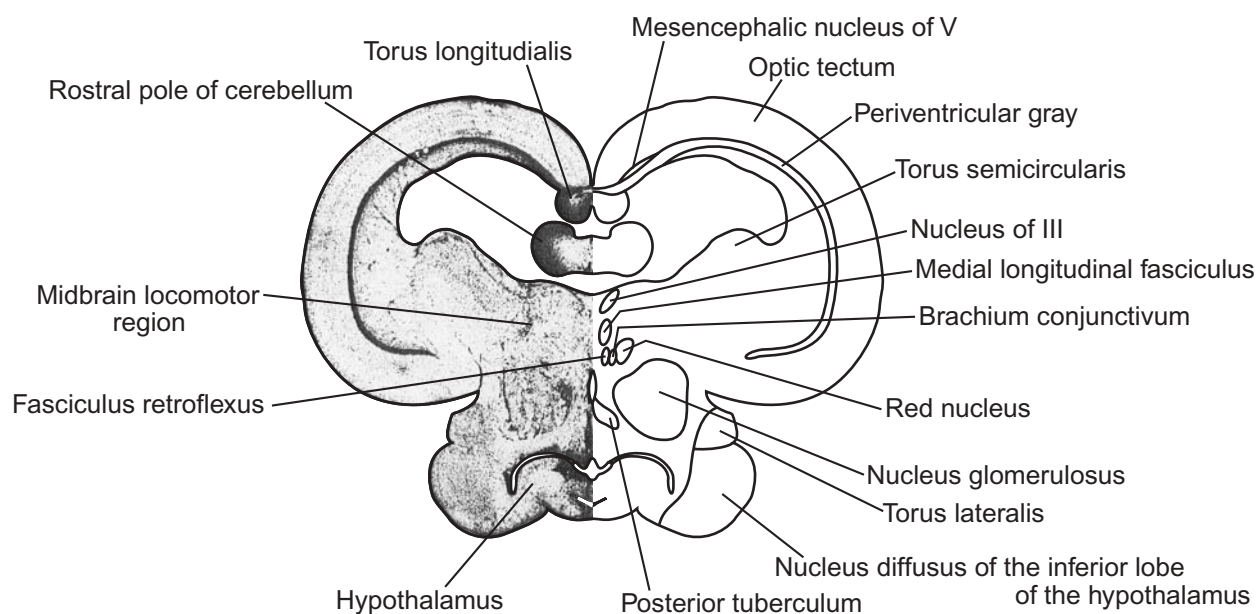


FIGURE 17-10. Transverse hemisection with mirror-image outline drawing through the tegmentum of a teleost fish (*Lepomis gibbosus*). Adapted from Parent et al. (1978) and used with permission of John Wiley & Sons.

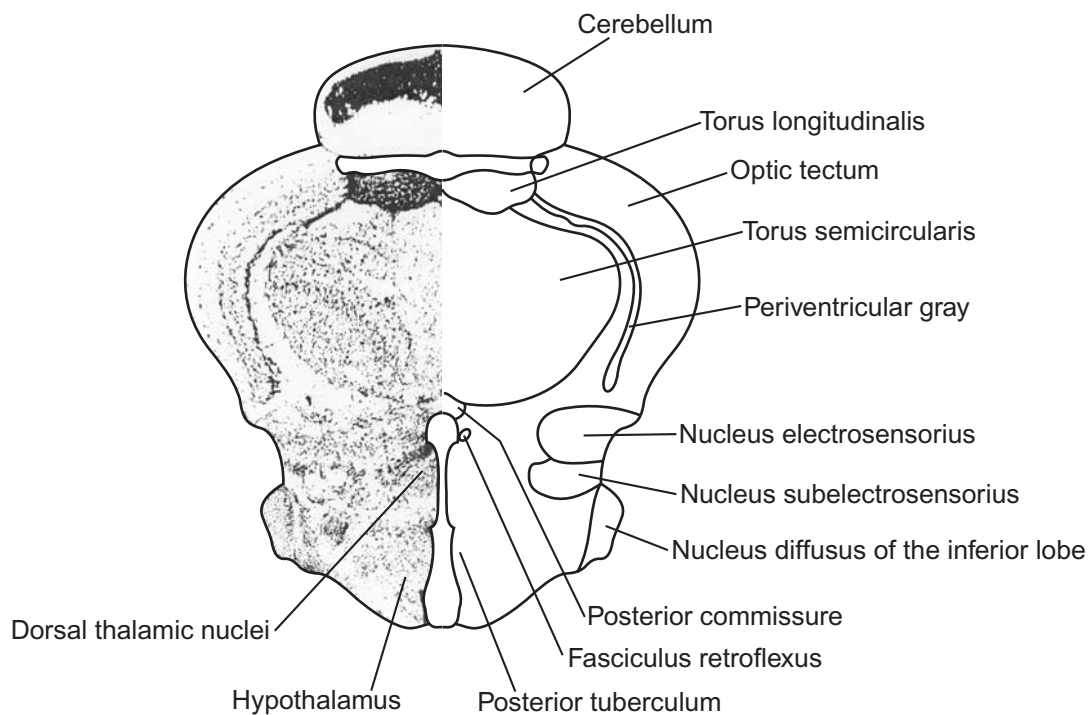


FIGURE 17-11. Transverse hemisection with mirror-image outline drawing through the tegmentum of a weakly electric gymnotiform fish (*Apteronotus leptorhynchus*). Adapted from Maler et al. (1991) and used with permission of Elsevier.

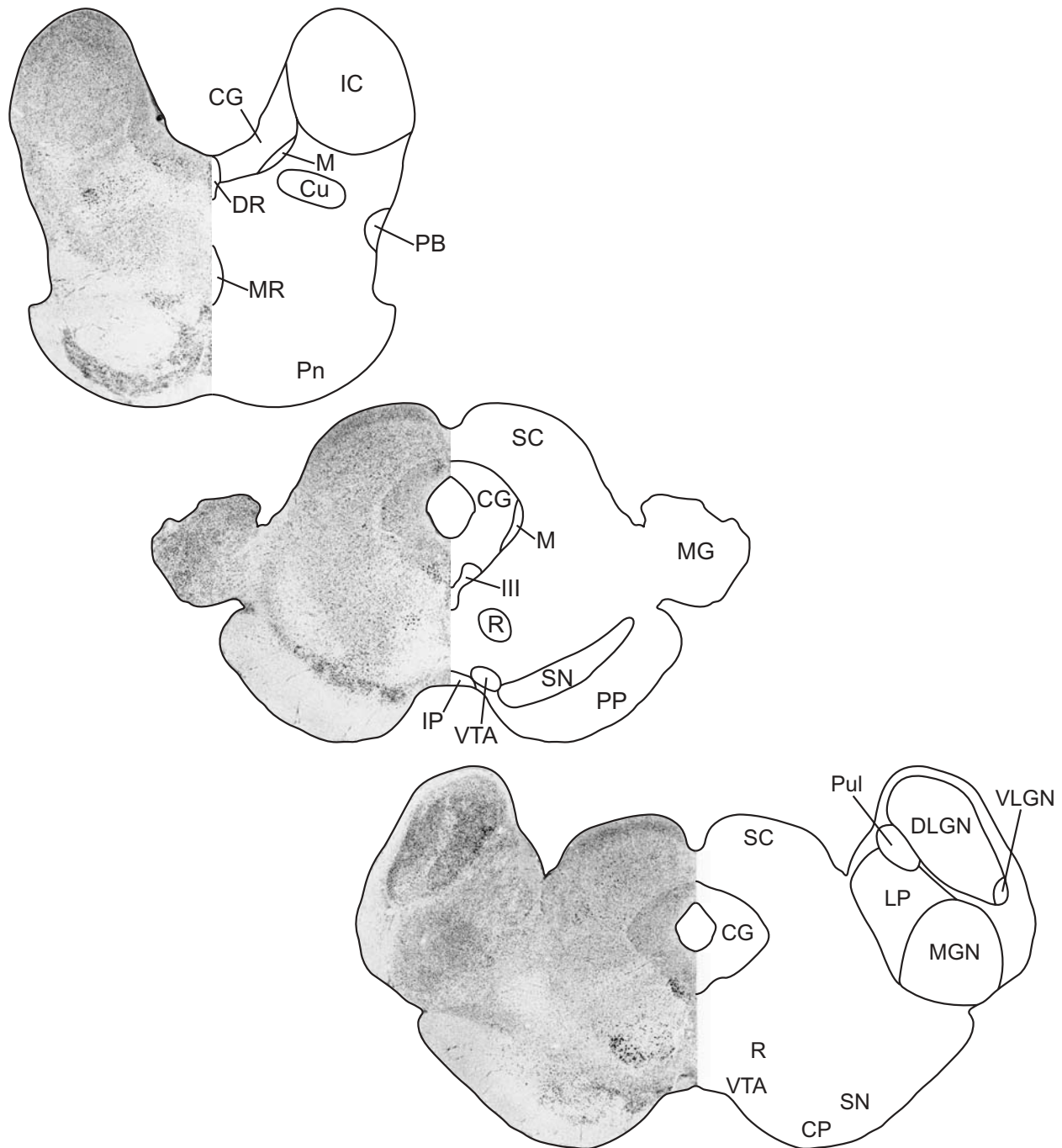


FIGURE 17-12. Transverse hemisections with mirror-image drawings through the tegmentum of a mammal (*Procyon lotor*). The upper section is most caudal. Abbreviations: CG, central gray; Cu, cuneiform nucleus; DR, dorsal raphe nucleus; IC, inferior colliculus; IP, interpeduncular nucleus; LG, dorsal lateral geniculate nucleus; M, mesencephalic trigeminal nucleus; MG, medial geniculate nucleus; MR, medial raphe nucleus; PB, parabigeminal nucleus; Pn, pontine nucleus; PP, pes pedunculi; R, red nucleus; SC, superior colliculus; SN, substantia nigra; VTA, ventral tegmental area; III, oculomotor nucleus. Photograph courtesy of Wally Welker.

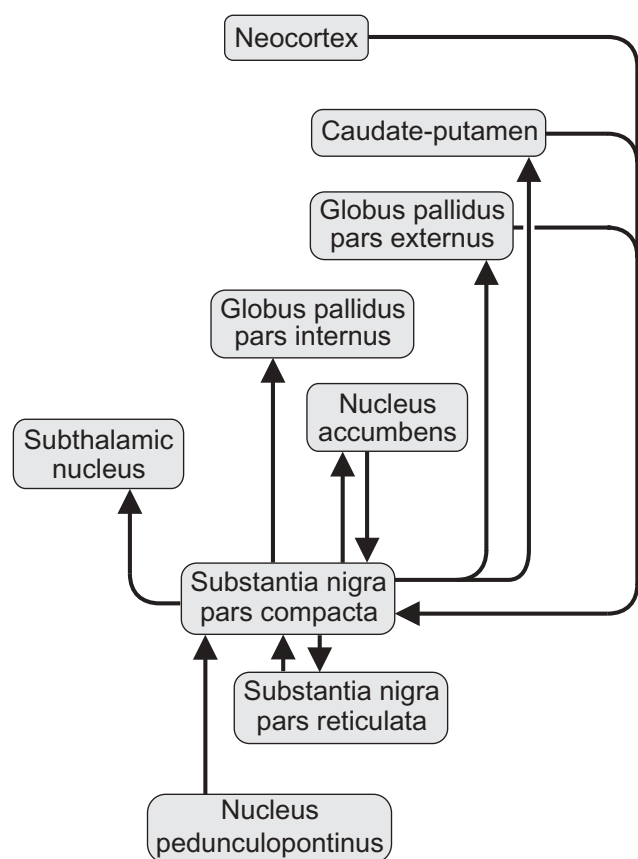


FIGURE 17-13. Some connections of the substantia nigra pars compacta in mammals.

tine nucleus (which relays cerebellar nuclear inputs to it). The dopaminergic inputs from the pars compacta to the dorsal striatum are crucial for regulating the activity of two circuits, or loops, that involve the dorsal thalamus, neocortex, and dorsal striatum, one of which is inhibitory and the other of which facilitates the initiation of movements. It is the balance between these two circuits that allows one to choose to be at rest without tremor or unwanted movements and then to initiate purposeful movements when desired.

The connections of the substantia nigra pars reticulata (Fig. 17-14) are somewhat different from those of the pars compacta. This GABAergic cell group receives inputs from components of the striatopallidal complexes and neocortex and is reciprocally connected with the substantia nigra pars compacta and a component of the ventral thalamus, called the subthalamic nucleus. The latter nucleus is a key component of the inhibitory loop mentioned above, which inhibits the production of involuntary movements. The substantia nigra pars reticulata also projects to nuclei in the dorsal thalamus, also part of the striatopallidal loops for movement regulation, and to the superior colliculus, in which it can influence descending collicular participation in the motor system.

The ventral tegmental area gives rise to ascending dopaminergic projections to the forebrain, some of which terminate in the dorsal and ventral striatum, ventral pallidum, hippocampal formation, amygdala, and medial parts of neocortex.

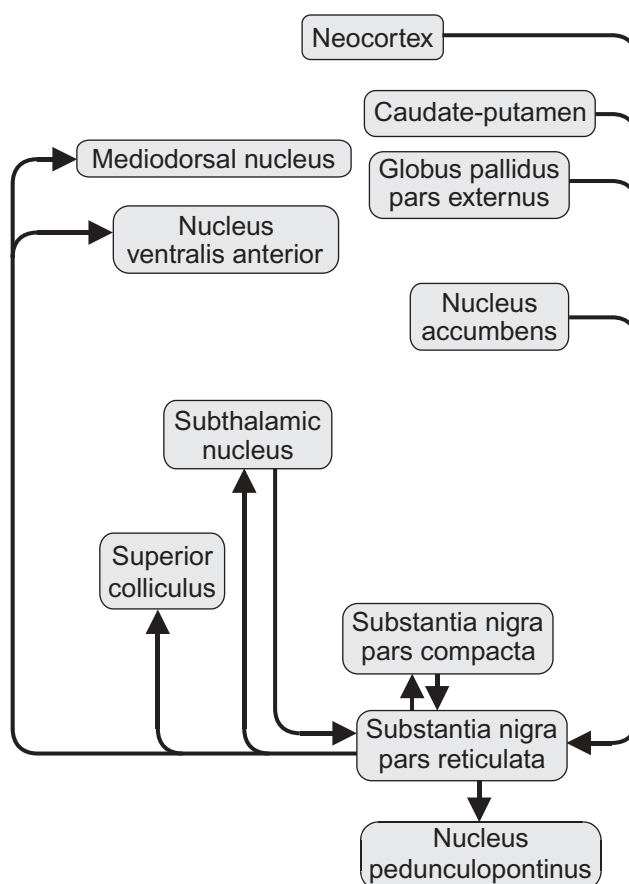


FIGURE 17-14. Some connections of the substantia nigra pars reticulata in mammals.

The projection to nucleus accumbens is the most prominent of its efferent projections and is in fact considered diagnostic for recognizing the territory of the nucleus accumbens itself. Within the brainstem, the ventral tegmental area projects to the raphe as well as to a number of other tegmental sites. Its sources of afferent projections include nucleus accumbens and the ventral pallidum, part of neocortex and limbic cortex, the amygdala, and, in the brainstem, the raphe and the interpeduncular nucleus.

The substantia nigra's ascending projection to the caudate-putamen is frequently referred to as the **nigrostriatal dopamine system**. This system has historically been viewed as essentially separate and different from the set of ascending projections of the ventral tegmental area to more medial, limbic related structures in the telencephalon. A new concept of the midbrain dopamine projection systems in mammals has recently emerged, however, that recognizes a more integrated mixture of pathways. A dorsal-ventral division of the combined set of the A9 and A10 cell groups, rather than the medial (A10) versus lateral (A9) nuclear divisions, is more consistent with the pattern of connections. The ventral parts of A9 and A10 project to the dorsal striatum, whereas the dorsal parts project to both limbic and striatal structures. The total set of ascending dopaminergic midbrain projections is referred to as the **mesotelencephalic system**, which is composed of the **mesostriatal** and **mesocorticolimbic systems**.

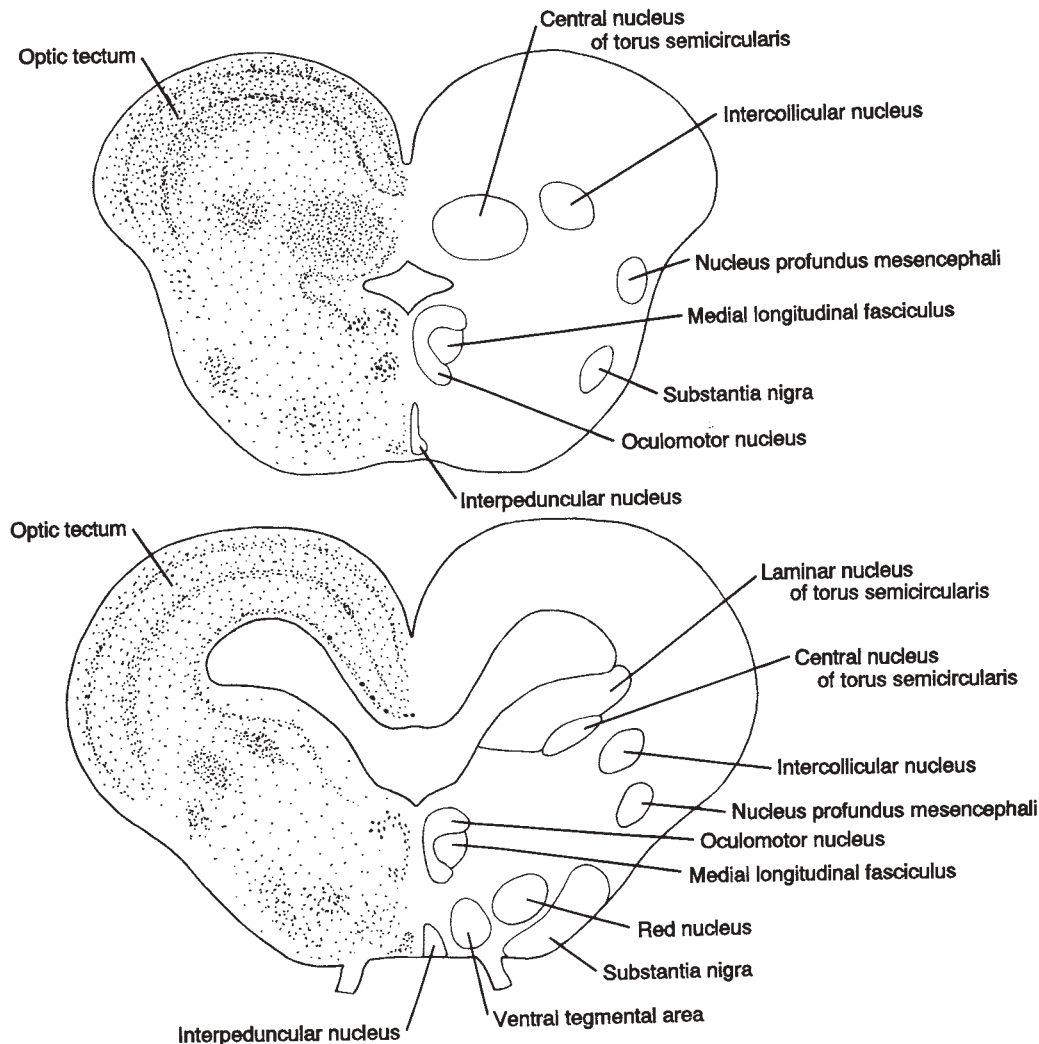


FIGURE 17-15. Drawings of transverse hemisections with mirror-image outline drawings through the tegmentum of a lizard (*Tupinambis nigropunctatus*). The more caudal section is at the top. Adapted from ten Donkelaar and Nieuwenhuys (1979) with additional data from Parent (1986). Cell bodies of the mesencephalic nucleus of the trigeminal nerve are indicated by the larger dots in the medial part of the optic tectum in the more rostral section. Used with permission of Elsevier.

The substantia nigra, ventral tegmental area, dorsal striatum, and nucleus accumbens have all been identified (although sometimes with differing terminology) in reptiles (Fig. 17-15) and birds (Fig. 17-16) on the basis of similar connections and/or the identification of similar neurotransmitters. The substantia nigra of birds was previously labeled as the pedunculopontine nucleus but is now correctly named. Some differences in connections occur, however, which reflect the separate evolutionary courses of the amniote radiations. We now want to consider one example of the variation that occurs in this system, which involves the relative topographic arrangements of one of the input systems to the midbrain dopamine-containing cell groups.

In mammals, reptiles, and birds, some of the fibers that arise in the striatum and project to the substantia nigra contain a neurotransmitter that is a peptide called substance P. There

are also substance P-containing afferent fibers to the ventral tegmental area, which, if they arise in the striatum, would constitute an additional, interconnecting pathway present in all groups of amniotes (not shown in Fig. 17-13). Differences occur in the degree to which the substance P-containing fibers overlap the area of the dopamine-containing cells in both the substantia nigra pars compacta and the ventral tegmental area. In lizards, turtles, and rats, there is very little overlap. In pythons, crocodiles, birds, and primates, there is extensive overlap (Fig. 17-17).

From this distribution, we cannot determine which trait (overlap or separation) of the substance P-containing fibers and the catecholamine-containing cells has been evolved multiple times. Outgroup comparisons suggest that a separation was the primitive condition for this system in ancestral vertebrates, as in both a lungfish and a cartilaginous fish, almost no overlap of

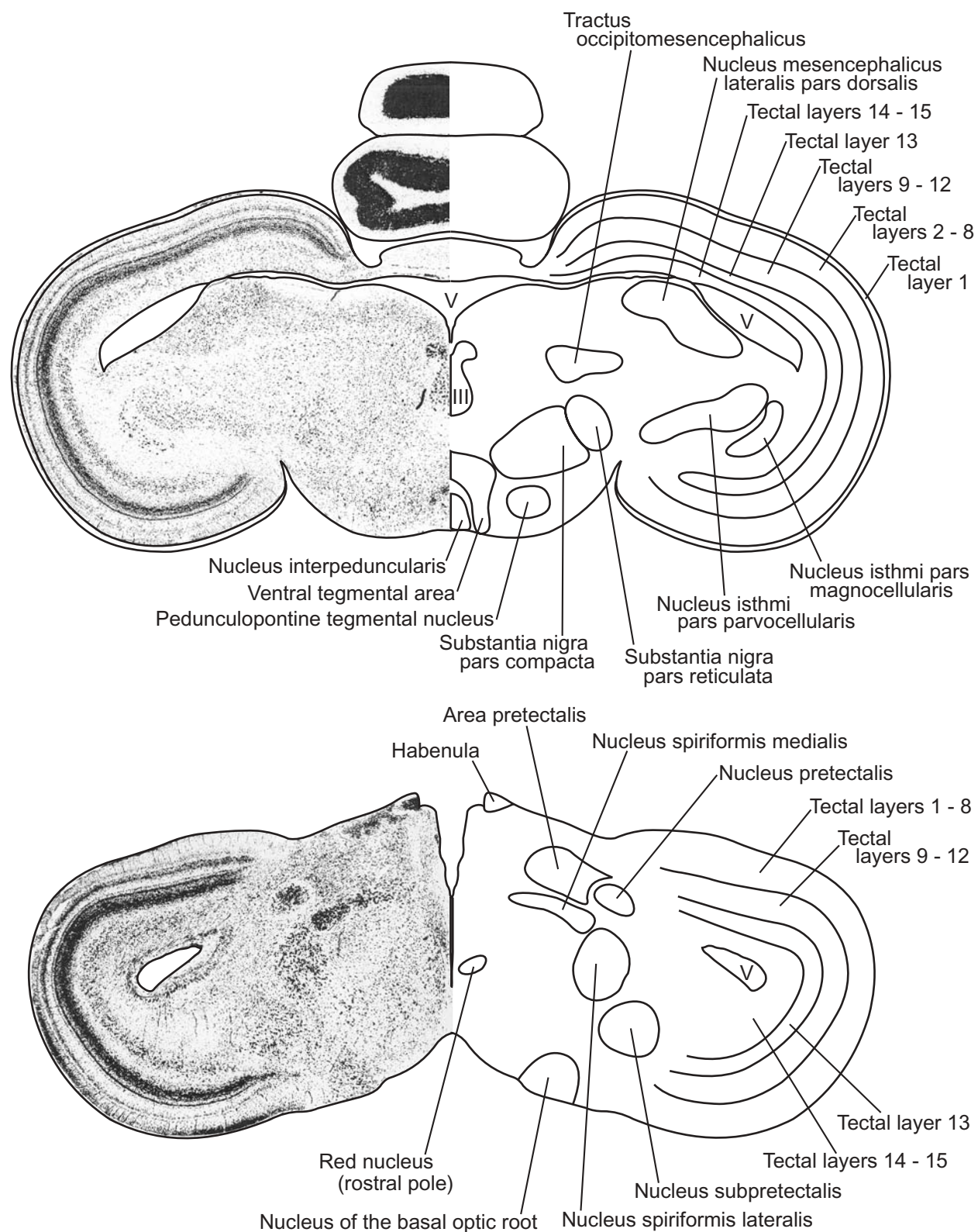


FIGURE 17-16. Transverse hemisections with mirror-image drawings through the tegmentum of the pigeon (*Columba livia*). Adapted from Karten and Hodos (1967) and used with permission of The Johns Hopkins University Press.

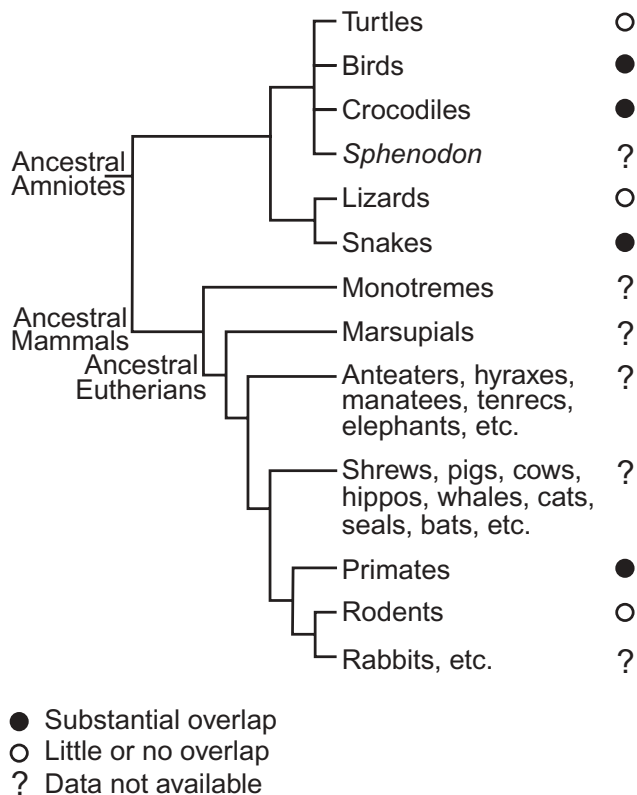


FIGURE 17-17. Dendrogram showing the distribution of substantial overlap (filled circles) versus little or no overlap (open circles) of substance P-containing fibers and catecholamine-containing cells in the substantia nigra and ventral tegmental area among amniotes. Question marks indicate no available data.

the afferent fibers and the cells occurs. Overlap has therefore evolved at least three separate times independently: in pythons, in the thecodont ancestors of crocodiles and birds, and in primates. Because the repertoires of movements in these groups are very diverse, it is hard to guess, at least for the moment, at the functional significance of greater overlap of substance P-containing fibers and catecholamine-containing cells in the substantia nigra and ventral tegmental area. In humans, the overlap is exceptionally extensive, and it is known that a loss of substance P occurs in cases of Huntington's and Parkinson's diseases.

One additional circuit needs to be discussed, as it is also related to the pathology of Parkinson's disease and is involved with the midbrain locomotor region that we discussed above. In mammals, the pedunculopontine nucleus lies next to the cuneiform nucleus (discussed above in relation to the midbrain locomotor region). The pedunculopontine nucleus projects to the pars compacta of the substantia nigra and receives descending projections from the cerebral cortex, striatum, and subthalamic nucleus. It is also present in reptiles and birds (see Fig. 15-6). In all amniotes, the pedunculopontine nucleus is characterized by its population of cholinergic neurons. In mammals, pathological over-activity of the neurons in the pedunculopontine nucleus and subthalamic nucleus (which contains excitatory, glutamatergic neurons and is discussed further in Chapter 24) can result from a decrease in the

dopaminergic input to the striatum, such as occurs in the early stages of Parkinson's disease. Since both the pedunculopontine and subthalamic nuclei project to the pars compacta of the substantia nigra, this over-activity can produce excitotoxic effects on the remaining dopaminergic neurons in the substantia nigra pars compacta and may thus contribute to the progression of the disease.

Evolutionary Perspective

A posterior tuberculum is present in lampreys, all cartilaginous fishes, all ray-finned fishes, lungfishes, and amphibians. The posterior tuberculum is thus a plesiomorphic feature of vertebrate brains. In all species studied, cells in the posterior tuberculum have been found to contain catecholamine.

In contrast, nuclei identified as the ventral tegmental area and substantia nigra are present only in two groups: the sharks, skates, and rays (but not in ratfishes) and the amniotes. The absence of these structures in all ray-finned fishes, lungfishes, and amphibians implies that they have been independently evolved in cartilaginous fishes and in amniotes.

Is the posterior tuberculum derived from the hypothalamus and its catecholamine-containing cells homologous to the A11 cell group of amniotes, or could the posterior tuberculum comprise a field homology or a serial homology to the area or areas that give rise to some or all of the A8–A10 mesencephalic cell groups in both cartilaginous fishes and amniotes? In the adults of cartilaginous fishes, the cells in the posterior tuberculum are not in a rostrocaudal continuum with those in the ventral tegmental area and substantia nigra. In adult specimens of amniotes, no posterior tuberculum has been found, although it has recently been identified within the posterior parencephalon (or p2 prosomeric segment) in a segmental analysis of the brain in chick embryos, and further studies may allow for its identification in adult mammals and other nonavian amniotes. Recent evidence on the substantia nigra in mammals indicates that it does not migrate during development from a more caudal region to its position in the adult, as previously believed, but may arise from the median proliferative zone within its own segmental sector in the mesencephalon, as does the ventral tegmental area. Whether the projection from the posterior tuberculum to the striatum in frogs is homologous (as a connection of serially homologous structures) or homoplasious to that of the substantia nigra to the striatum in amniotes is unresolved. Few other data on posterior tubercular connections are currently available. Further embryological studies of the derivation of these nuclei in both cartilaginous fishes and amniotes and further studies of the connections of the posterior tuberculum will contribute to the resolution of this problem.

Variation in the pattern of projections to and from the substantia nigra and ventral tegmental area needs to be further examined in a number of species. At least six different neurotransmitters have been identified in this system of projections in mammals, and additional studies on the distribution of these neurotransmitters in nonmammalian vertebrates can be used to determine what specific changes and modifications this part of the motor control system has undergone in various radiations over evolution and how these changes are correlated with function.

TORUS LATERALIS

Group I

A cell group that might correspond to the torus lateralis has not been identified in lampreys or sharks. In nonteleost ray-finned fishes, the nucleus of the torus lateralis forms a bulge on the edge of the brain ventral to the optic tectum (Figs. 17-3). In reedfishes, sturgeons, and gars, the torus lateralis is relatively large in size, and it is enormous in the bowfin (Fig. 17-4). In reedfishes, the torus lateralis projects to the telencephalon, but other connections are still unknown. A torus lateralis has not been identified in lungfishes or amphibians.

Group II

A torus lateralis has not been identified in hagfishes. The nucleus is present in most teleosts (Fig. 17-10) but is more modestly sized than in nonteleost ray-finned fishes. There is no known homologue of the torus lateralis in amniotes.

Evolutionary Perspective

The torus lateralis may be unique to ray-finned fishes. Its only known efferent connection is to the telencephalon in reedfishes, and its afferent connections are unknown. Additional studies of its connections may indicate that a homologue of this nucleus exists in other taxa, but for the moment, its function and origin remain an enigma.

TORUS SEMICIRCULARIS

The torus semicircularis is the structure in the midbrain that receives ascending lateral line and auditory fibers. It is variable in both size and complexity and reflects the degree of development of the auditory system and both the mechanosensory and electrosensory components of the lateral line system. The torus semicircularis is an excellent example of how form is correlated with function.

Group I

In lampreys, the torus semicircularis (Fig. 17-1) lies ventral to the optic tectum along the ventral surface of the tectal ventricle. The cells form a lamina along the ventricle. The lateral line system in lampreys receives auditory inputs and is also both mechanoreceptive and electroreceptive. The torus semicircularis receives inputs from a variety of sources in addition to the octavolateral system, including the reticular formation, optic tectum, and diencephalon. It projects to sites within the diencephalon and reticular formation.

The torus semicircularis is also in receipt of auditory, mechanoreceptive, and electroreceptive information in squalomorph sharks and ratfishes. In squalomorph sharks (Fig. 17-2), part of the torus semicircularis forms a slight bulge along the lateral surface of the ventricle. The major toral nucleus, the **lateral mesencephalic nucleus**, is partially migrated and lies in a more lateral position. Ascending projections from lateral line nuclei in the medulla project to the lateral mesencephalic

nucleus via the lateral line lemniscus. The lateral mesencephalic nucleus is functionally subdivided in that electrosensory lateral line input is distributed to the more dorsolateral part of the nucleus, while mechanosensory lateral line input is distributed to its more ventromedial part. The most ventral part of the lateral mesencephalic nucleus may receive ascending auditory projections via the same lemniscal pathway.

The torus semicircularis forms a prominent bulge on the ventricular surface in nonteleost ray-finned fishes (Fig. 17-3). Ascending octavolateral fibers form the lateral lemniscus and terminate within subdivisions of the torus semicircularis. While reedfishes and sturgeons are electroreceptive, gars and bowfins are not. The electroreceptive system was apparently lost in the common ancestor of gars, bowfins, and the large teleost radiation.

Within the sarcopterygian radiation, the crossopterygian fish *Latimeria* and lungfishes have both mechanoreceptive and electroreceptive lateral line systems. All amphibians have a lateral line system in their aquatic larval stages, and both mechanoreceptive and electroreceptive components are present in urodele and larval apodan (gymnophionan) amphibians. Only a mechanoreceptive lateral line system is present in larval anurans. During metamorphosis, however, the lateral line systems are lost in most anuran (including the frog *Rana*) and apodan amphibians. The lateral line organs are not functional in air. A few species, including the African clawed frog *Xenopus*, retain the lateral line system, and this retention is correlated with an aquatic lifestyle and/or aquatic breeding.

In amphibians with the lateral line system, the information (electroreceptive and/or mechanoreceptive) is relayed to the torus semicircularis along with auditory information via the lateral lemniscus. The torus semicircularis in frogs is quite large and is composed of several subdivisions: the **principal**, **laminar**, and **magnocellular nuclei** (Fig. 17-6). In the frog *Xenopus*, which retains the mechanoreceptive lateral line system, the large principal nucleus receives ascending auditory projections, while the magnocellular nucleus receives lateral line projections. A small area is also present between these nuclei, which receives ascending somatosensory information for the integration of touch stimuli. In the frog *Rana*, which has no lateral line system in the adult, the auditory input is also to the principal nucleus, but the ascending somatosensory projection extends throughout the magnocellular nucleus. In all frogs, the laminar nucleus receives projections from the magnocellular and principal nuclei, and cells in the laminar nucleus also have dendrites that extend into these two nuclei. The laminar nucleus is the main source of projections from the torus semicircularis to the optic tectum and to the auditory area of the dorsal thalamus, the central thalamic nucleus.

With the emergence of vertebrates onto land, the lateral line system could no longer be used to detect predators or prey or to communicate. Hence, an increased use was made of both vision and sound. The only amphibians that use sound for communication are frogs, and the development of the auditory parts of the brain in frogs reflects the importance of the system.

Sound communication has been extensively studied in frogs. This system is useful as a model for the processing of sound and its content by the central nervous system, as there are a set of rather constant and simple signals used for specific situations, most relating to territory and reproduction. Males

produce an “advertisement” call when ready to breed, and these calls are answered with either “phonotaxic” calls from receptive females or “antiphonal” calls from other males. Males produce “courtship” calls when approached by females. “Release” calls are made by females improperly clasped during amplexus (mating) or by clasped males, and “aggressive” calls are used by males confronting each other. “Distress” calls are made when a frog is seized by a predator. Each call can be characterized in terms of waveform and pulse rate, and each set of calls is species specific. Studies of central processing of the stimuli in the brainstem nuclei and midbrain, as well as information on individual mating selection, speciation (behavioral mechanisms of isolation), and variation of behavior with habitat have all been done on this system of sound communication. The releasing response, for example, has been found to be mediated by cells in the region of the anterodorsal tegmental nucleus, which lies immediately ventral to the torus semicircularis.

Group II

A torus semicircularis has not been identified in hagfishes. The lateral line system in hagfishes is solely mechanoreceptive and confined to the head. Studies of ascending auditory and lateral line projections, which could reveal the location of the torus semicircularis, have not yet been done.

In squalomorph sharks, one nucleus, the lateral mesencephalic nucleus, is present lateral to the ventricular bulge of the torus itself; however, the galeomorph sharks, skates, and rays have several distinct nuclei in this region (Fig. 17-8). These nuclei are collectively called the **lateral mesencephalic nuclear complex (LMN)**. Ascending fibers from the electrosensory lateral line nuclei project via the lateral lemniscus to the **lateral nucleus** of the LMN. Mechanosensory lateral line projections terminate in the **dorsomedial nucleus**, and auditory projections terminate in the **ventromedial nucleus** of the complex. A more rostral nucleus in the complex, the **anterior nucleus**, does not receive direct, ascending octavolateral projections but instead receives an electrosensory input from the lateral nucleus.

In most teleost fishes, the torus semicircularis (Fig. 17-10) is well developed, but the nuclear cell masses that receive ascending octavolateral input are not migrated laterally away from the bulge in the ventricular surface as they are in cartilaginous fishes. The torus semicircularis projects to a nucleus in the dorsal thalamus, the central posterior nucleus, which, in turn, projects to the telencephalon. The central posterior nucleus also projects back to the torus semicircularis. The torus semicircularis has reciprocal connections with several other structures (the medullary reticular formation, the contralateral torus semicircularis, and the anterior tuberal nucleus in the hypothalamus), and it receives a direct projection from an area in the caudal telencephalon. Additionally, the torus semicircularis is reciprocally connected with the optic tectum, and these projections are topographically mapped so that the visual map of space from the tectum is in register with the auditory and lateral line maps of space in the torus semicircularis and vice versa (see Chapter 18).

Although electroreception was lost in the ancestral stock of gars, bowfins, and teleosts, an electroreceptive lateral line

system was apparently subsequently reevolved independently in several groups of teleosts. This has occurred separately in two groups of osteoglossomorphs (see Chapter 4)—notopterids and mormyrids—and in two groups of ostariophysans (Euteleostei)—gymnotids and silurids.

In some electroreceptive teleosts, the torus semicircularis is massive. A section through this region in a weakly electric gymnotid fish (*Apteronotus*) is shown in Figure 17-11. In these fishes, the dorsal part of the torus semicircularis receives electrosensory input, and the ventral part receives auditory and mechanoreceptive lateral line inputs. The torus semicircularis in *Apteronotus* has a number of connections similar to those in other teleosts; however, it also projects to a large electrosensory nucleus in the caudal diencephalon called **nucleus electrosensorius**. Nucleus electrosensorius, in turn, projects to another nucleus called the **prepacemaker nucleus**, which modulates the discharges of the electric organ for signals associated with courtship, aggression, and other behaviors. The location of nucleus electrosensorius is roughly similar to the location of the electrosensory-receptive, anterior nucleus of the lateral mesencephalic nuclear complex (LMN) in cartilaginous fishes with elaborated brains; thus, these structures may be an example of convergence.

The lateral line electrosensory system is absent in all amniote vertebrates, having been lost in ancestral amniotes with the transition from water to land. In all amniotes, the torus semicircularis (inferior colliculus) receives ascending auditory projections via the lateral lemniscus. Its major efferent projection is to auditory nuclei in the dorsal thalamus, which, in turn, relay the information to the telencephalon (to auditory cortex and part of the pallial amygdala in mammals and to a part of the dorsal ventricular ridge in reptiles and birds).

In mammals, the auditory midbrain roof is called the **inferior colliculus** (Fig. 17-12). It receives ascending auditory inputs directly from the cochlear nuclei and also from other auditory system nuclei in the brainstem, including the superior olivary nuclei and the nuclei of the lateral lemniscus. The inferior colliculus comprises a large, egg-shaped central nucleus and two smaller regions, a pericentral, or dorsal, nucleus, which projects to the central nucleus, and an external, or lateral, nucleus. Within the central nucleus, both the neuron cell bodies and the afferent fibers are arrayed in a laminar arrangement, and the low to high frequencies of sound inputs are aligned in an ordered sequence from one lamina to the next in a dorsal to ventral direction, respectively, across the nucleus. The central nucleus is the conduit for the main pathway to auditory cortex. It projects to the ventral division of the medial geniculate nucleus, MGNv, which in turn projects to primary auditory cortex. The pericentral and external nuclei of the inferior colliculus also contribute to the ascending auditory pathway but via other divisions (medial and dorsal) of the medial geniculate nucleus that project predominantly to association auditory cortical areas and (via the medial division) to the lateral nucleus of the amygdala. Auditory cortical areas also project back to the inferior colliculus but predominantly to the pericentral and external nuclei rather than directly to the central nucleus.

Studies of the inferior colliculus in echolocating bats have shown that some of its neurons respond to biologically important features of sounds, such as duration. The latter class of

neurons is particularly tuned to durations that are in the range of the bat's echolocation calls. Responding to duration-sensitive and other species-specific sound parameters may be a general feature of the inferior colliculus across vertebrates. Additionally, the superior colliculus participates in auditory responses in echolocating bats and probably in other vertebrates as well. It receives auditory input from the inferior colliculus and is responsible for the generation of head and pinnae turning movements toward the source of the sound.

In reptiles (Fig. 17-15), the auditory midbrain roof is called the torus semicircularis. In turtles, it contains a laminar nucleus and a **central nucleus**, with the latter being the main source of auditory projections relayed rostrally to the dorsal thalamus. Central, laminar, and superficial nuclei have been identified in lizards and central and external nuclei in crocodiles. In all reptiles, the central nucleus is the main source of thalamic projections. In birds, the torus semicircularis is commonly called the **nucleus mesencephalicus lateralis dorsalis** (Fig. 17-16), or MLd. It contains a central nucleus, which is the major source of auditory projections to the dorsal thalamus. The auditory midbrain is somewhat specialized in owls, which rely heavily on auditory cues for hunting prey in the dark. At least three subnuclei are present—superficial, external, and central. The external nucleus projects to the deeper layers of the optic tectum, which plays a crucial role in influencing the development of the map of auditory space based on visual input.

Evolutionary Perspective

A torus semicircularis has been identified in all radiations of vertebrates with the exception of hagfishes, where its presence has not yet been investigated. This structure is clearly one that was evolved very early in the vertebrate radiation. Among anamniotes, the size and complexity of the torus semicircularis are directly correlated with the degree of elaboration of the lateral line system, particularly its electrosensory component. The electrosensory lateral line system is thought to have evolved multiple times independently, and thus, the correlated augmentation of the torus semicircularis in these cases is an example of convergence.

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18

Optic Tectum

INTRODUCTION

The roof of the midbrain is known as the tectum. In most vertebrates, particularly those with a well-developed visual system, the tectum is dominated by a retinorecipient region called the **optic tectum** (Fig. 18-1) or, as it is often called in mammals, the **superior colliculus** (Fig. 18-2). Although its major input is from the retina, the optic tectum is more than just a visual processing structure. The three major hallmarks of its organization are (1) it is multisensory (visual, auditory, somatosensory, and where present, infrared-sensory, electrosensory, and/or magnetic sense), (2) the inputs from different systems are organized as “maps” of the external world or the body, and (3) these maps are in register with each other; for example, a given location on the map of external visual space corresponds to the same location in external auditory space. One of the major functions of the optic tectum is to localize a stimulus in space and to cause the animal to orient to the stimulus by moving its neck and/or its eyes.

OVERVIEW OF TECTAL ORGANIZATION

In nearly all vertebrates, the optic tectum is a structure of substantial size located on the dorsal surface of the mesencephalon. At its core is a ventricle that is connected to the main ventricular system of the brain. Only mammals and hagfishes lack this tectal ventricle. The cellular organization of the tectum consists of a series of layers from its outer surface to the

periventricular core. Because the number of layers varies across taxa and because the tectum has been studied by many different investigators who have used their own variations of names and numbers for the tectal layers, the nomenclature of the tectum can be a challenge for the newcomer to this area of the brain. Where possible, we have used a simplified approach in which the tectum is divided into three major zones, or groups of layers: **superficial**, **central**, and **periventricular**. Figure 18-3 illustrates these three zones in a ray-finned fish. Within the superficial zone, the position of the main layer of afferent fibers from the retina, the **stratum opticum**, can be either superficial or deep to the rest of the zone. Likewise, the fibrous part of the periventricular zone, called the **deep white zone**, or **stratum album profundum**, lies either immediately superficial or deep to the periventricular gray zone. The terminology for the superficial zone is relatively straightforward, since the term superficial is used in most taxa. The terminology for the central and periventricular zones overlaps in different nomenclatural systems, however. The central zone can alternatively be called the intermediate zone or, more rarely, the medial zone. Alternatively, the periventricular zone has been called the deep zone, and in mammals, its deepest part is frequently called the central gray. Thus, the word “central” can be ambiguous when used out of context in tectal terminology. The “central zone” and the “stratum griseum centrale,” which is part of the central zone, are not the same as the “central gray,” which is part of the periventricular zone.

The morphology of tectal neurons has been studied in a number of different animals using the Golgi technique. In this histological process, for an unknown but fortuitous reason, only a few of the many neurons become impregnated with silver, so the morphology of the neuron soma and most or all

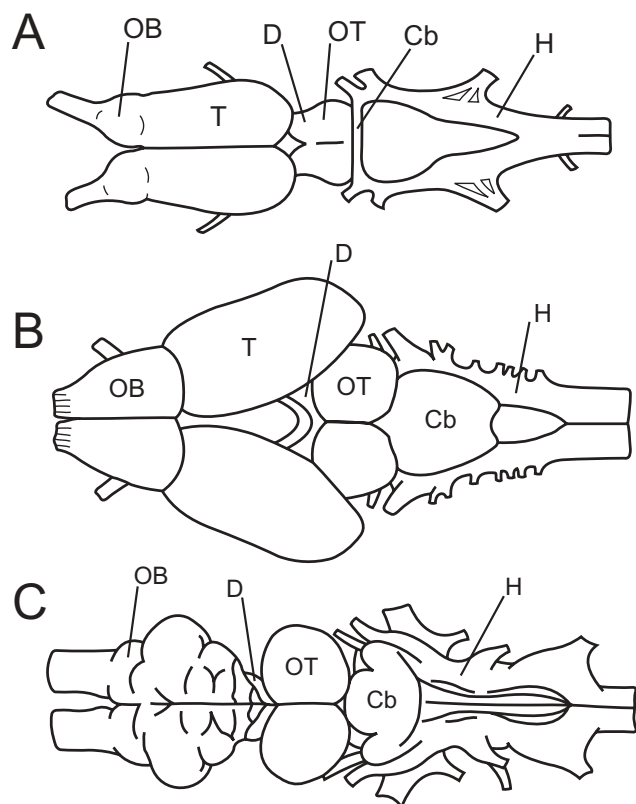


FIGURE 18-1. Dorsal views of the brains of a mudpuppy, *Necturus maculosus* (A), a turtle, *Chrysemys picta* (B), and a ray-finned fish, *Amia calva* (C), showing the position of the optic tectum (OT) in relation to the olfactory bulb (OB), telencephalon (T), and diencephalon (D) rostrally and the cerebellum (Cb) and hindbrain (H) caudally. Mudpuppy and turtle drawings adapted from Northcutt (1979b) and *Amia* drawing adapted from Butler and Northcutt (1992). Used with permission of The University of Chicago Press and S. Karger AG, Basel, respectively.

of its processes can be seen and is unobscured by the surrounding neurons. This method is particularly well suited for the study of laminated structures, such as the optic tectum.

Golgi studies have revealed many different cell types, including a population of tectal neurons that have radially (i.e., centrifugally) oriented dendrites. These neurons are called **piriform cells** in reference to their pear-shaped cell bodies. The dendrites of the piriform cells often extend through most of the tectal layers. Each population of incoming axons tends to be confined to a particular, tangentially oriented band, or sublayer, within the optic tectum. This physical arrangement allows for incoming information from different systems to be segregated on the dendritic shafts of individual neurons (Fig. 18-4). The very limited degree of branching of the dendrites of the radially oriented, piriform neurons also allows for a precise, point-to-point pattern of termination for each incoming system.

These morphological features provide for a high degree of precision of spatial mapping in the optic tectum, as well as permit the different sensory systems to be spatially in register. The mapping of sensory information in the optic tectum is in

topologic, if not topographic, order, due to transformations of the information along the visual pathway through the layers of the retina and the optic nerves and tracts. Here, we use the term topographic in the same sense as used in the literature in sensory system analyses. An example of topography is shown in Figure 18-5; successive points along the edge of a door in your visual field, which fall on the retina, will be kept in topographic order through the visual pathway to your optic tectum. A similar illustration of visual field mapping onto the optic tectum of a fish is shown in Figure 18-6.

Visual information, carried by retinal cell axons, terminates primarily in the superficial zone of the optic tectum. Somatosensory information, relayed by nuclei in the hindbrain, terminates in the deeper half of the central tectal zone. Within the optic tectum, given points in space are mapped topographically and in register for the two systems. For example, touch from the face is mapped in register with the superior and nasal visual fields, corresponding to what would be seen in looking up and in looking toward the nose; touch from the body is similarly mapped in register with what would be seen in looking to the side and down. In those species of snakes that have an infrared (IR)-detecting system (see Chapters 2 and 11), an IR map of space is also present in the optic tectum. This map is correlated with the visual map, particularly in the most rostral part of the optic tectum, which maps the area directly in front of the snake. Because this frontal field is important for striking prey, a greater area of the optic tectum is devoted to this part of the field for IR input than for visual input. In a number of different vertebrate taxa, the tectum also participates in a system to topographically analyze magnetic information, allowing long-distance migrations to be carried out accurately and/or ranges to be circumscribed (see Box 18-1).

OVERVIEW OF TECTAL CONNECTIONS

The major source of afferents to the optic tectum is the retina. The optic tectum is also the target of descending projections from the forebrain, especially from the telencephalic pallium and nuclei in the thalamus and pretectum. In some vertebrates, direct projections from the telencephalic pallium reach the optic tectum, while input from nuclei in the subpallium is relayed to the optic tectum through the diencephalon. Reciprocal commissural input to the optic tectum arises in the contralateral optic tectum. Nucleus isthmi (see Chapter 16) also has reciprocal connections with the optic tectum. Much of the tectal input and output is topographically organized. Ascending projections from the spinal cord and a number of brainstem regions provide topographic somatosensory and motor feedback information to the optic tectum.

The optic tectum sends ascending fibers to nuclei in the diencephalon. Most of these projections are bilateral, with the greater number of fibers projecting to the ipsilateral diencephalon. As will be discussed in detail in Chapter 22, the major ascending pathways are to one or more nuclei in the dorsal thalamus that receive little if any retinal input and relay projections to parts of the telencephalon. The optic tectum also projects more sparsely to a dorsal thalamic nucleus that

BOX 18-1. Magnetoreception and the Optic Tectum

Many animals are able to orient to the magnetic field of the earth's surface. The role of the trigeminal nerve in detecting magnetic cues is now well established (see Box 11-1). A number of behavioral studies have provided convincing evidence that magnetic field orientation plays a key role enabling animals to migrate long distances with great accuracy. For example, Kenneth Lohmann and his co-workers studied hatchling loggerhead sea turtles. From Florida, these hatchlings normally enter the ocean and swim to the North Atlantic gyre, which is a current that encircles the Sargasso Sea. The gyre sweeps clockwise off the eastern coasts of parts of South and North America and then over to the western coasts of Europe and the northern part of Africa. The hatchlings' survival is highly dependent upon their remaining within this gyre for several years. If they stray outside the gyre, they may either die from the colder water temperatures farther north or stray far south of their normal range and their home coastal breeding ground. When the hatchlings were exposed to magnetic fields produced under laboratory conditions that replicated those found in the gyre and the northern and southern territories flanking the gyre, they oriented in such a way as to remain within the gyre. This study thus provides a direct demonstration of orientation to naturally relevant magnetic field stimuli. It also shows that the orientation ability and behavior are innate. The hatchlings immediately respond to light and magnetic cues in order to get into the water and to then orient for swimming within the North Atlantic gyre.

Visual stimuli in combination with magnetic information have been implicated in navigational ability. John Phillips and his co-workers have studied the orienting behavior of salamanders in this regard. They have shown that magnetic orientation is influenced by light—both a short-wave and a long-wave component. The influence of the light is mediated not by the retina but rather by the pineal photoreceptors. Light, via retinal reception, is also a crucial component of magnetic orientation for birds, as has been shown by Wolfgang and Roswitha Wiltschko and their co-workers, as well as by others in this field. European robins require light cues and magnetite-based magnetoreception for correct migratory orientation (see Chapter 2).

The sites of magnetic sensory information processing within the brain are largely uncharted. As discussed in Chapter 2, however, the retinal photoreceptors may be involved, and recent work by the Wiltschkos and others has indicated involvement of the optic tectum [as well as the nucleus of the basal optic root (see Chapter 20)] in magnetic orientation. The participation of the optic tectum in this system is highly consistent with its role in spatial orientation for visual, somatosensory, auditory, and other stimuli and its neuronal architecture and known functional capabilities. Pavla Němec and his co-workers recently combined well-established experimental techniques in an ingenious way to demonstrate the role of a specific population of

tectal neurons in magnetoreception in a mammal. In the Zambian mole rat (*Cryptomys anselli*), they examined the pattern of neuron cell bodies expressing the transcriptional regulatory protein c-Fos under different conditions of nest building or resting in an unfamiliar environment and under different magnetic field conditions. Within the superior colliculus, they found that cells within the outer sublayer of the intermediate gray layer and also within the deep gray layer expressed increased levels of c-Fos in an unspecific way associated with the novelty of an unfamiliar environment. In contrast, cells within the inner sublayer of the intermediate gray layer expressed increased c-Fos in correlation with variations in the magnetic field. Of particular interest, animals building nests in a constant magnetic field showed increased c-Fos in cells in this sublayer within the mediorostral part of the superior colliculus. In the condition of nest building combined with periodically changing magnetic fields, weaker c-Fos expression resulted but over a larger area within the tectum, i.e., throughout most of the rostral half of the superior colliculus. These results indicate that a magnetic field of a given polarity is the key stimulus and, further, that the magnetic representation within the superior colliculus is organized in a topographic fashion, mapping the external magnetic space, just as the visual and other sensory representations are mapped. Such a topographic map would be a highly plausible neural substrate for the interaction of light and magnetic cues in orientation behaviors.

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BOX 18-1. Magnetoreception and the Optic Tectum—cont'd

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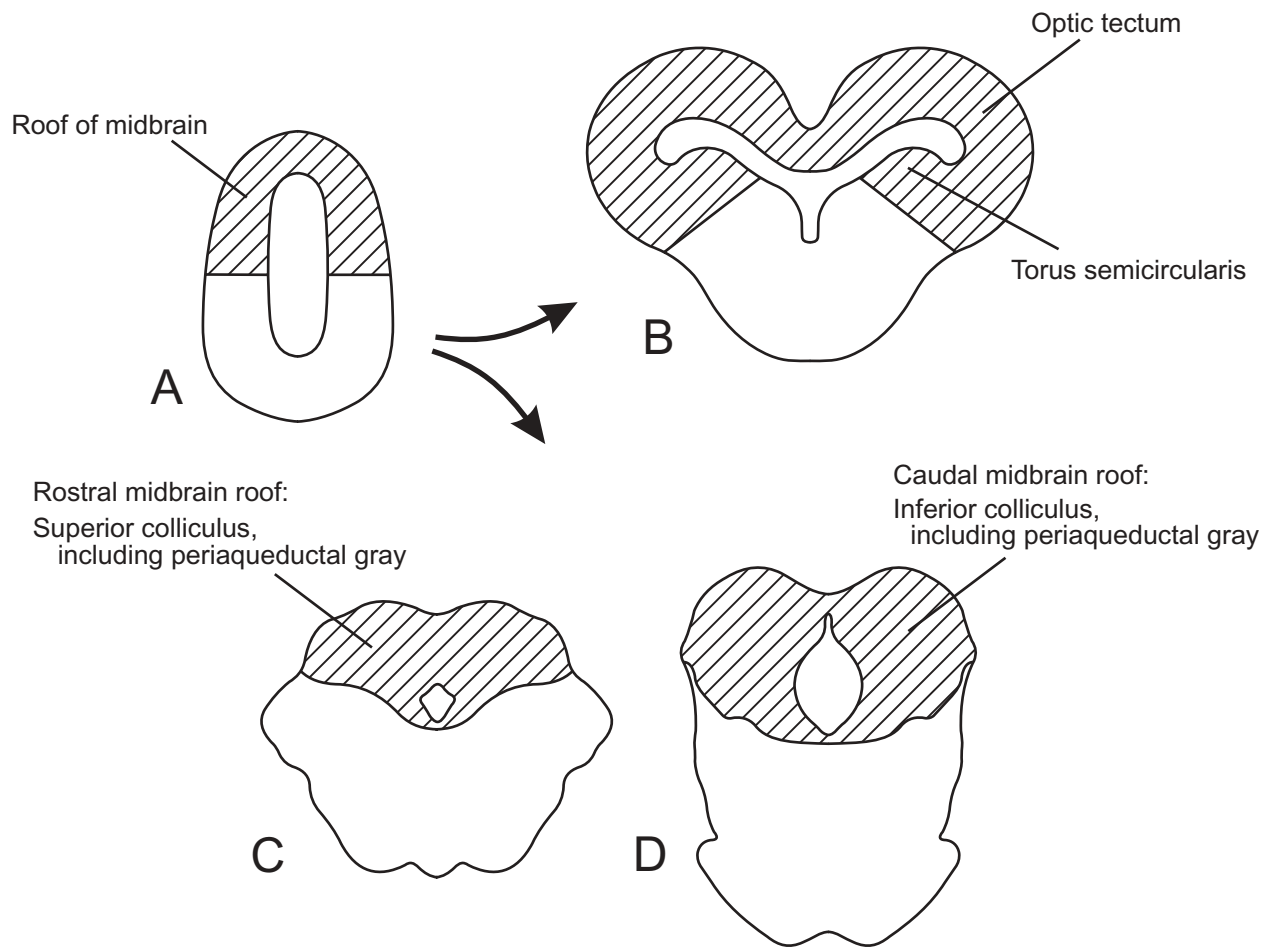


FIGURE 18-2. Schematic drawings of transverse sections through the roof of the midbrain in a generalized vertebrate embryo (A) that gives rise in nonmammalian vertebrates (B) to the optic tectum dorsally and the torus semicircularis ventrally and that gives rise in mammals to the superior colliculus rostrally (C) and the inferior colliculus caudally (D).

receives a substantial retinal projection and, in turn, projects to another part of the telencephalon. Thus, multiple major ascending pathways for visual information to the telencephalon are present.

Descending projections of the optic tectum are organized so that motor responses to sensory stimuli are appropriately oriented in space. Most descending tectal projections are to

ipsilateral sites, although a minority of fibers crosses to the contralateral brainstem. The three major tectal projection sites are regions of the midbrain tegmentum that are associated with motor functions, the reticular formation, and the rostral spinal cord. The optic tectum initiates motor commands that control sequences of movements directed toward a specific location in space. These commands reach the spinal cord through tegmen-

tal and reticular pathways, as well as via direct tectospinal pathways.

THE OPTIC TECTUM IN GROUP I VERTEBRATES

Lampreys

In lampreys, as in other vertebrates with laminar brains, most of the cell bodies of tectal neurons lie in the periven-

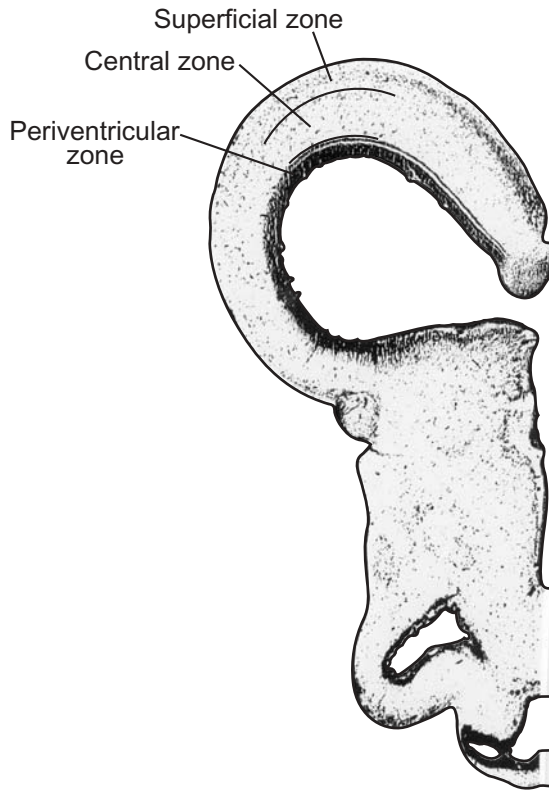


FIGURE 18-3. Transverse hemisection through the left side of the midbrain in the ray-finned fish *Amia calva*.

tricular gray zone (Fig. 18-7). A deep white zone (not labeled) lies just superficial to the periventricular gray zone, and some neuron cell bodies are scattered within the central and superficial zones.

The optic tectum contains a variety of neuronal types based on their dendritic trees. Piriform cells with radially oriented dendrites (Fig. 18-8 a and b) are present in the optic tectum, as are neurons with more horizontally oriented dendrites (Fig. 18-8 c and d). Cells with more complex patterns of dendritic branching, such as stellate cells, are also present (see Figure 18-8 e).

The retina projects to the optic tectum via the optic tract, which enters the optic tectum from a superficial position, and the individual retinal ganglion cell axons terminate in the superficial and central tectal zones (Fig. 18-9). The retinal terminations are heavier in the superficial zone than in the central zone. Piriform cells in the periventricular gray zone, such as that in Figure 18-8 b, receive a retinal input on the more distal portion of their dendrites.

A sparse projection from the spinal cord also reaches the optic tectum. These fibers terminate along the ventral border of the optic tectum (Fig. 18-9). Presumably, the optic tectum in lampreys gives rise to ascending and descending projections, but most of these pathways remain to be studied. It is known that the optic tectum, along with other structures in the diencephalon and mesencephalon, contributes projections to the reticular formation of the rhombencephalon.

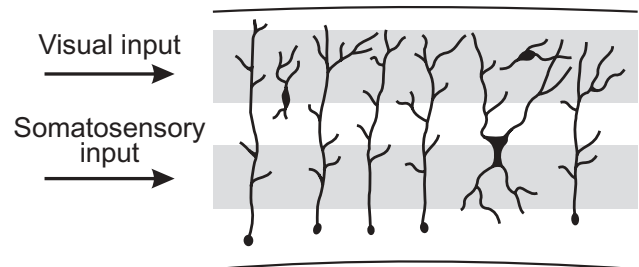


FIGURE 18-4. Segregation of afferent input on different parts of the dendritic shafts of individual tectal neurons. The retinal (visual) and somatosensory areas of termination are indicated by shading.

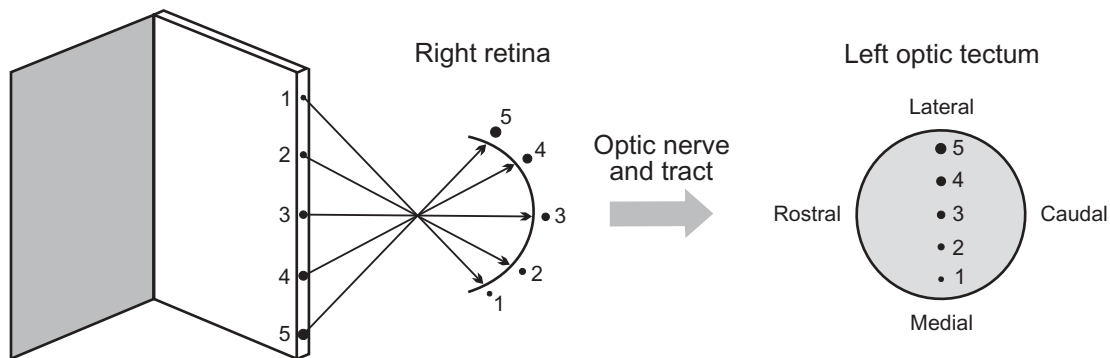


FIGURE 18-5. Maintenance of topographic order in the visual pathway from, in this example, the edge of a door to the retina of the eye, in the axons of the optic nerve and in their respective points of termination in the optic tectum.

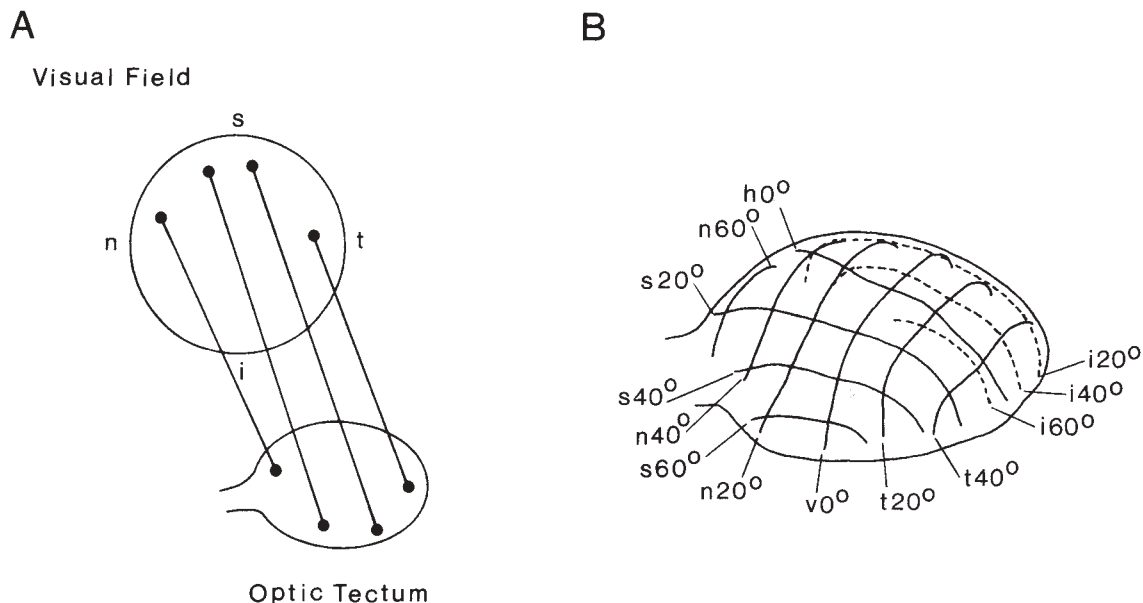


FIGURE 18-6. A: Schematic diagram of the mapping of points in the visual field onto a dorsal view of the optic tectum. B: Projection of the left visual field onto the dorsal surface of the right optic tectum. The optic tectum in both A and B is oriented so that lateral is toward the top, medial toward the bottom, rostral toward the left, and caudal toward the right. Abbreviations: s, superior; i, inferior; n, nasal (medial); t, temporal (lateral); h, horizontal; v, vertical. Adapted from Vanegas (1983).

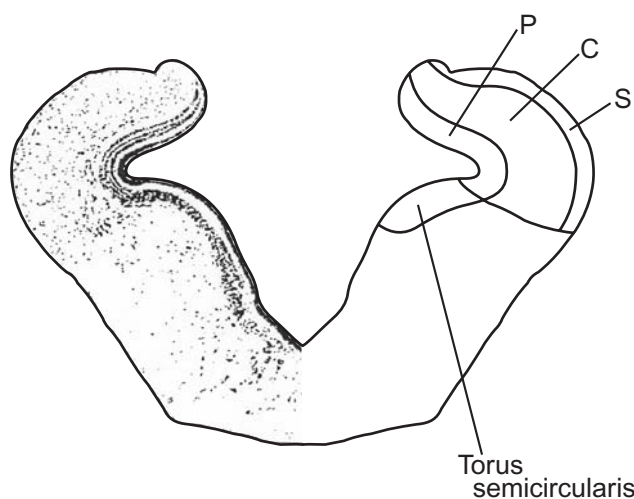


FIGURE 18-7. Transverse hemisection with mirror-image drawing through the left midbrain of a lamprey (*Petromyzon marinus*). Adapted from Kennedy and Rubinson (1977) and used with permission of John Wiley & Sons. In this and some subsequent figures, S, C, and P indicate the superficial, central, and periventricular zones of the optic tectum.

Squalomorph Sharks and Ratfishes

In the optic tectum of squalomorph sharks, such as *Squalus*, neuronal cell bodies are located predominantly in the periventricular gray zone (Fig. 18-10), although limited migration into the central zone occurs. In squalomorph sharks, most of the periventricular cells are piriform in shape and have radi-

ally oriented dendrites that extend into the central and superficial zones. In ratfishes, approximately 90% of the cell bodies of tectal neurons are confined to the periventricular gray zone. The central zone consists almost exclusively of heavily myelinated fibers, and the superficial zone consists of a superficial marginal layer, retinal fibers, and neuropil.

The optic tectum receives projections from the retina that terminate in the superficial zone. Most of the retinal fibers course along the deep border of the superficial zone, rather than running over the surface of the optic tectum, to reach their points of termination. Other connections of the optic tectum have been studied only in sharks with elaborated brains and in skates. It is likely that cartilaginous fishes with laminar brains have generally similar inputs to the optic tectum from the telencephalon, contralateral tectum, and spinal cord, as well as similar efferent projections to the diencephalon and to the more caudal parts of the brainstem. All of these pathways need to be investigated in squalomorph sharks and in ratfishes.

Nonteleost Ray-Finned Fishes

In all ray-finned fishes, the optic tectum can be divided into superficial, central, and periventricular gray zones, as in other vertebrates. A deep white zone of fibers is also present just superficial to the periventricular gray zone. In nonteleost ray-finned fishes, the largest collection of neuronal cell bodies is in the periventricular gray zone, and the cells form multiple, distinct layers (Fig. 18-11). Small, piriform cells with radially directed dendrites are abundant in the periventricular gray zone (Fig. 18-12 e-i). Cells with dendrites oriented horizontally are also present in the optic tectum (Fig. 18-12 a and d), as are

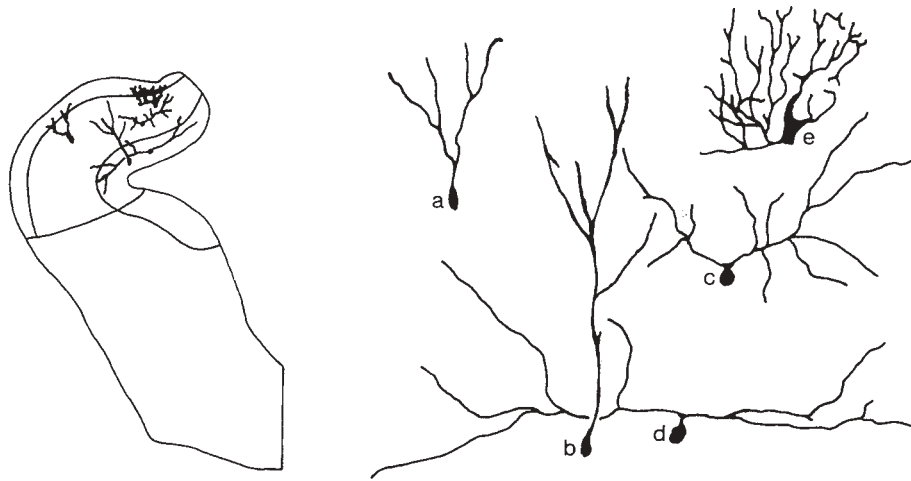


FIGURE 18-8. Neurons in the optic tectum of a lamprey as revealed with the Golgi method. A drawing of a left transverse hemisection is shown on the left for the orientation and location of the neurons shown on the right in an enlarged format. Data from Ariëns Kappers et al. (1967).

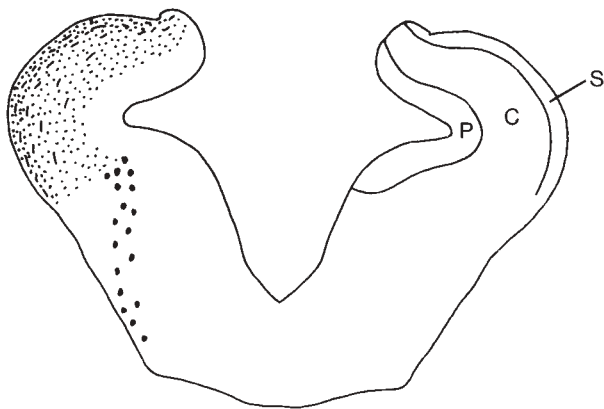


FIGURE 18-9. Retinal (small stippling) and spinal inputs (larger dots) to the optic tectum in a lamprey shown on the left side in a drawing of a transverse section. Data from Kennedy and Robinson (1977) and Ronan and Northcutt (1990).

a variety of cell types with dendrites radiating in multiple directions (Fig. 18-12 b, c, j, and k).

Retinal fibers, as shown on the left in Figure 18-13, terminate primarily in the superficial tectal zone, with a few also entering the more superficial part of the central zone. Other afferent projections to the optic tectum originate from a diverse array of nuclei in the telencephalon, diencephalon, and brainstem. The sources of tectal projections in the brainstem include nucleus isthmi, the locus coeruleus, the reticular formation, and the cerebellum. Unusually in a paddlefish (which, with sturgeons, is a member of the Chondrostei, as discussed in Chapter 4), the optic tectum also receives direct input from the electrosensory dorsal octavolateral nucleus, which projects to the optic tectum in addition to the torus semicircularis (see Chapter 17) and a lateral mesencephalic

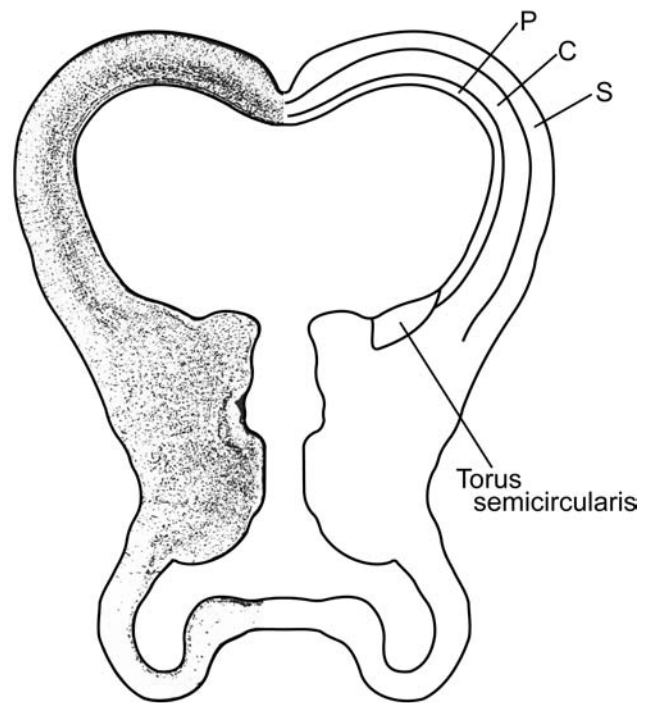


FIGURE 18-10. Transverse hemisection with mirror-image line drawing through the left midbrain of a squalomorph shark (*Squalus acanthias*). Adapted from Northcutt et al. (1988) and used with permission of John Wiley & Sons.

nucleus. The direct electrosensory octaval connection is consistent with the organization and function of the deeper part of the optic tectum as a topographically mapped, multisensory-motor integrative center.

The efferent projections of the optic tectum are also diverse. Ascending tectal projections terminate in a number of

different nuclei in the diencephalon. Of critical importance for visual perception are two nuclei in the dorsal thalamus that receive ascending tectal projections. The optic tectum projects sparsely to a nucleus in the dorsal thalamus, nucleus anterior, that is also in receipt of retinal projections and that, in turn, projects to the telencephalon. The optic tectum projects densely to another dorsal thalamic nucleus, the dorsal posterior nucleus, which does not receive retinal projections but does, in turn, also project to the telencephalon. The presence of at least two, separate, dorsal thalamic nuclei that receive tectal projections, one of which also receives substantial retinal projections, with both projecting to the telencephalon, is a widespread feature of visual system organization in vertebrates

(Fig. 18-14) and will be discussed further below. However, in at least some ray-finned fishes, the main visual pathway from the optic tectum to the telencephalon may involve a nucleus of the posterior tuberculum, which is a caudal part of the diencephalon (see Chapter 20). In the bichir, the optic tectum sends a substantial projection to a nucleus called **nucleus medianus of the posterior tuberculum**, which in turn projects to the dorsolateral pallium in the telencephalon (formerly called P2/P3; see Chapter 19).

Many of the descending projections of the optic tectum are reciprocal in nature, such as those to nucleus isthmi and the reticular formation. The optic tectum also projects to the nucleus lateralis of the valvula cerebelli. The latter nucleus is a

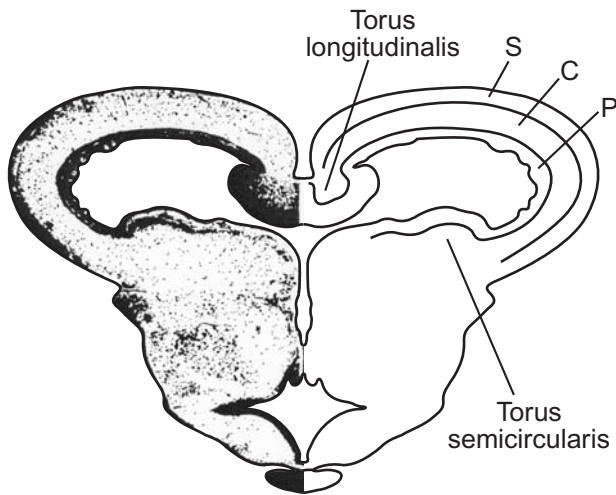


FIGURE 18-11. Transverse hemisection with mirror-image drawing through the left midbrain of a longnose gar (*Lepisosteus osseus*). Adapted from Northcutt and Butler (1976).

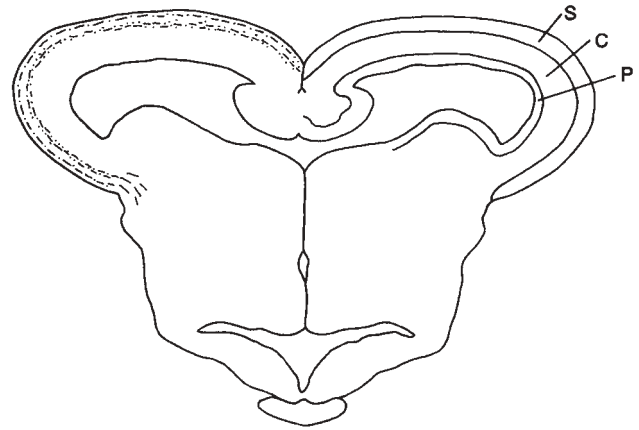


FIGURE 18-13. Retinal (small stippling) input to the left optic tectum in a longnose gar shown in a drawing of a transverse section. Data from Northcutt and Butler (1976).

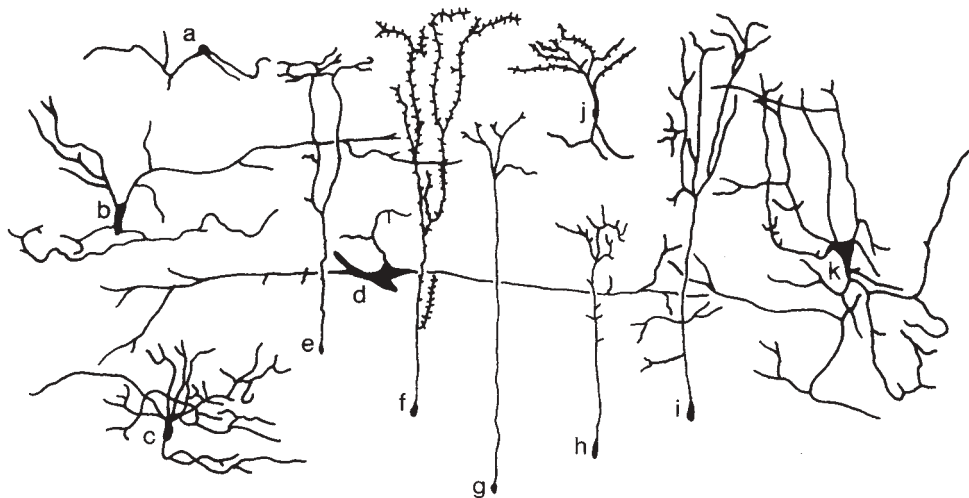


FIGURE 18-12. Neurons in the optic tectum of the bowfin (*Amia calva*) as revealed with the Golgi method. Data from Northcutt (1983).

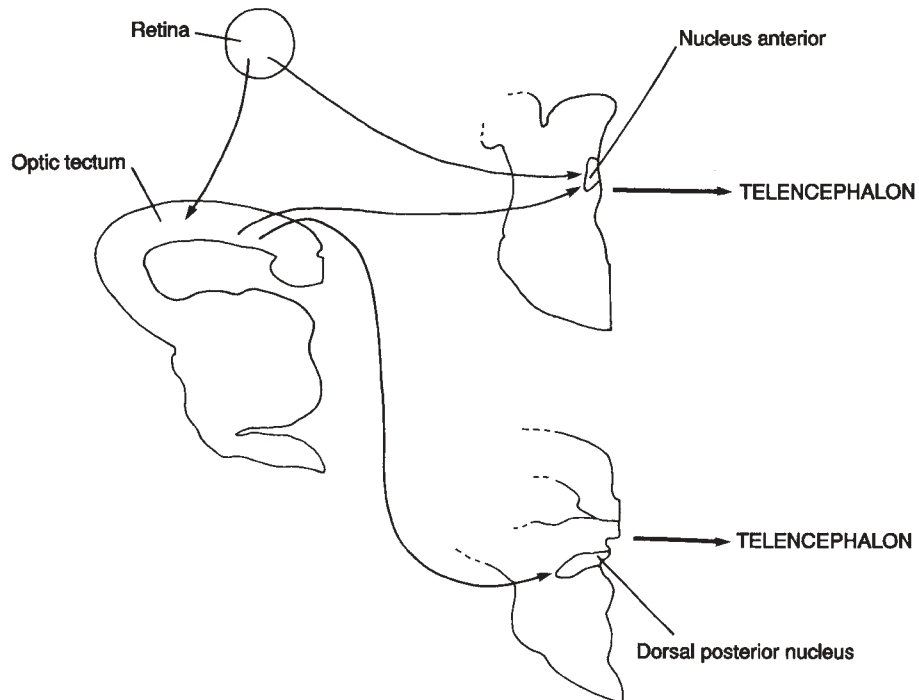


FIGURE 18-14. Diagram showing two pathways by which visual information reaches the telencephalon in ray-finned fishes and some other groups of anamniote vertebrates. The retina projects directly to both the optic tectum and to a dorsal thalamic nucleus, nucleus anterior. The optic tectum projects lightly to nucleus anterior and more robustly to a second dorsal thalamic nucleus, the dorsal posterior nucleus. Nucleus anterior and the dorsal posterior nucleus project to separate regions within the telencephalon.

precerebellar nucleus that projects to the cerebellum. Reciprocal projections between the two tectal lobes cross the midline via the tectal commissure.

Ray-finned fishes have a structure associated with the optic tectum that is not present in other vertebrates. This structure, which is a rostral extension of the cerebellum (see Chapter 14), is called the **torus longitudinalis**. It consists of a rostrocaudally extending bulge of the tectal layers that lies along the midline and protrudes into the tectal ventricle (Fig. 18-11). The torus longitudinalis appears to be part of the circuitry that affects descending motor output through the optic tectum.

Amphibians

In the optic tecta of salamanders (and similarly in lungfishes among the sarcopterygians), neuronal cell bodies are almost totally confined to the periventricular gray zone (Fig. 18-15). In frogs, some of the neuron cell bodies are migrated more peripherally into the central and superficial zones (Fig. 18-16). Small piriform neurons (Fig. 18-17 a–c) with radially oriented dendrites are numerous in the tectal layers in frogs. Among other cell types, larger, multipolar cells with far-reaching dendrites, called **ganglionic cells** (Fig. 18-17 d and e), are also present.

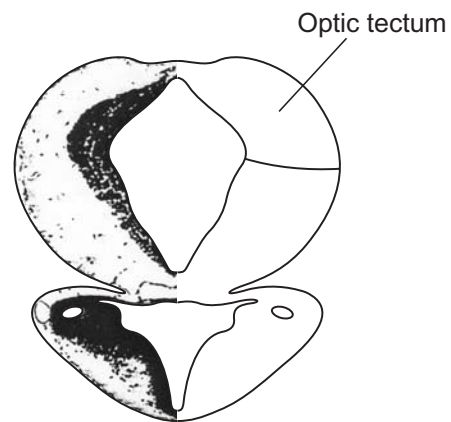


FIGURE 18-15. Transverse hemisection with mirror-image line drawing through the left midbrain of a salamander (*Salamandra salamandra*). Adapted from Fritzsche (1980) and used with kind permission of Springer Science and Business Media.

In amphibians, the retinal projections to the optic tectum terminate in the superficial zone and are topographic. Most studies of tectal afferents have been done in frogs, where projections from nuclei in the diencephalon, the contralateral

optic tectum, nucleus isthmi, several areas within the tegmentum, and the dorsal part of the cervical spinal cord have been identified. These nuclei, with the exception of nucleus isthmi (discussed below), project to the central zone of the optic tectum.

In frogs, input to the optic tectum from the telencephalon is via a multisynaptic relay in the diencephalon. In salamanders, a direct projection has been found from the telencephalon to the optic tectum. It terminates in the central zone, deep to the retinal input in the superficial zone.

As in ray-finned fishes, projections to the optic tectum from nucleus isthmi are topographic, and the optic tectum

projects reciprocally and topographically to nucleus isthmi. The tectal cells that project to nucleus isthmi are primarily piriform neurons in the periventricular gray zone (Fig. 18-17 c). Some tectal ganglionic cells project to nucleus isthmi as well. All of the neurons in nucleus isthmi project exclusively to the optic tectum. Their axons terminate in the superficial tectal zone, overlapping the zone of termination of retinal cell axons. The isthmal input to the optic tectum, which is cholinergic, modulates tectal responses to visual stimuli. Nucleus isthmi is believed to play a role in allowing the animal to avoid large, threatening stimuli and to attack smaller, prey-sized stimuli. These behavioral sequences have been studied extensively and will be discussed further below.

Efferent projections of the optic tectum are widespread. Ascending projections to the dorsal thalamus and pretectum arise from small piriform neurons in the central zone (such as in Fig. 18-17 b). These projections terminate in a number of different nuclei, including the anterior lateral nucleus in the dorsal thalamus, which does not receive a direct retinal projection. It projects to the telencephalon. A second, dorsal thalamic nucleus, nucleus anterior, receives a substantial retinal input and a minor tectal input, both via direct projections and via a relay through another nucleus in the posterior thalamus. It also projects to the telencephalon.

The commissural and descending projections of the optic tectum in frogs are similar to those in other vertebrates and serve motor output functions. These projections arise from pir-

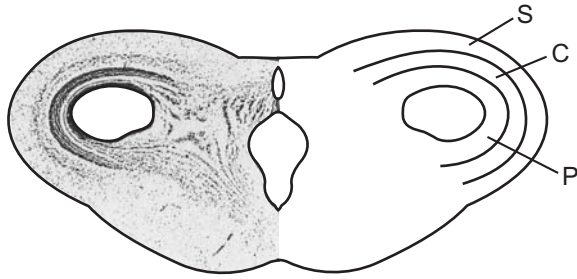


FIGURE 18-16. Transverse hemisection with mirror-image drawing through the left midbrain of a bullfrog (*Rana catesbeiana*). Adapted from Wilczynski and Northcutt (1983) and used with permission of John Wiley & Sons.

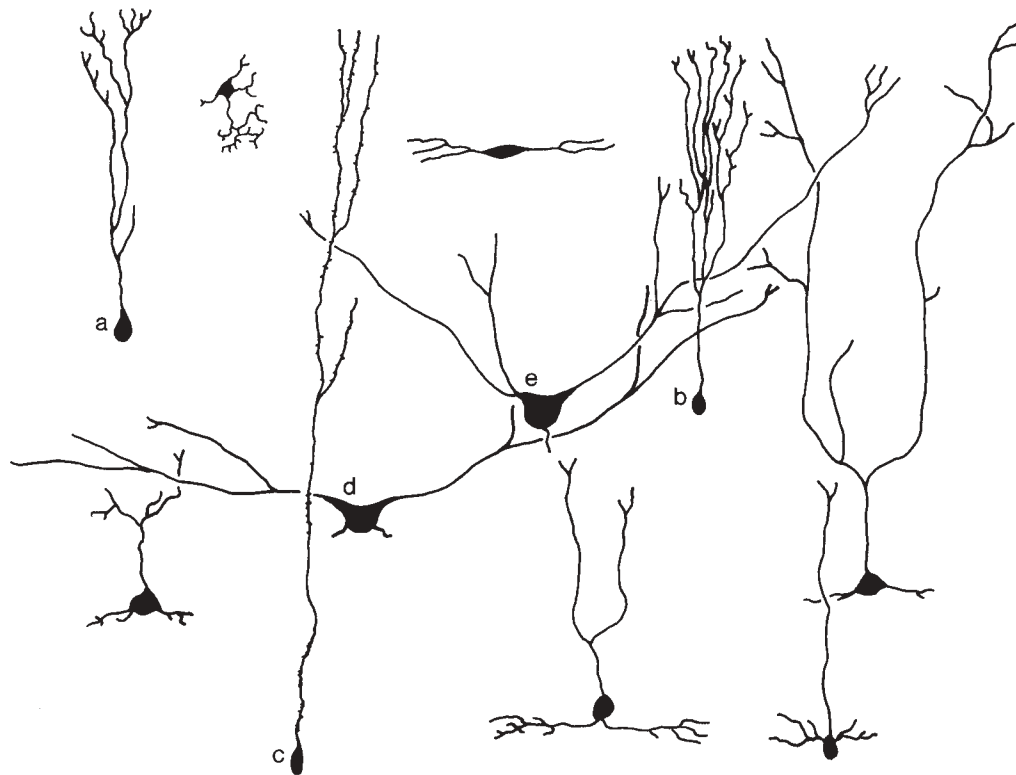


FIGURE 18-17. Neurons in the optic tectum of a frog as revealed with the Golgi method. Data from Székely (1971).

iform and large ganglionic neurons (Fig. 18-17 c and d) in the periventricular gray zone and the deeper part of the central zone.

The optic tectum projects to the contralateral tectum, nucleus isthmi (as discussed above), the magnocellular nucleus of the torus semicircularis, and multiple sites in the tegmentum. The latter include nucleus profundus mesencephali (see Fig. 17-6), the anterodorsal tegmentum (Fig. 17-6), the tegmental central gray, and the nuclei of the extraocular muscles and the medial longitudinal fasciculus. More caudally extending tectal projections reach the reticular formation and other sites in the hindbrain as well as the rostral part of the spinal cord. In salamanders, the tectum projects both directly and multisynaptically to the hypoglossal nucleus and thus is involved in the visuomotor control of tongue movements. Thus, there are multiple pathways by which tectal neurons influence neurons in the spinal cord—directly and by relays through the tegmentum and the reticular formation.

A number of behavioral studies designed to define the function of various afferent and efferent tectal connections have been carried out in frogs. In fact, the optic tectum of frogs is now regarded by many as a model for tectal function in anamniotes. For example, when a prey-sized black disk, small enough to resemble a fly or other similarly appetizing insect, is presented to a normal frog in a particular part of the visual field, the frog spatially orients toward the stimulus (employing the topographically mapped retinal input to the optic tectum) and then attempts to capture and eat it (employing spatially mapped motor patterns initiated by the optic tectum). When a predator-sized black disk, one that is large enough to resemble a threatening stimulus, is placed in a particular part of the visual field, the frog orients away from this potential threat and leaps away, using similar tectal mechanisms. These responses do not involve learning; they are determined by the neuronal circuitry of the optic tectum and its related structures and pathways. Such natural behaviors allow one to ask experimental questions about both the sensory processing (size, location, movement, etc. of the disk) and the motor output (reaction, orientation, attack or escape, etc.) functions of the optic tectum.

In response to prey-sized stimuli, for example, the optic tectum initiates a program of behavioral events—orienting, fixating, snapping, gulping, and wiping—that are regulated both in space and, sequentially, in time. The program can be modified after it has been initiated, if, for example, a barrier to the stimulus is encountered or the position of the stimulus changes. The various parts of the program are facilitated by ipsilateral input from the telencephalon and carried out by the tectotegmental, tectoreticular, and tectospinal pathways. They are continually adjusted in response to tectal inputs from the retina, forebrain, nucleus isthmi, contralateral optic tectum, brainstem feedback systems, and other sources.

Responses of avoidance to threatening stimuli are initiated by nuclei in the posterior thalamus and pretectum that project to the optic tectum. If these nuclei are surgically destroyed, the frog is “disinhibited” and readily attacks large stimuli as if they were prey. The normal tectal programs for avoidance postures and leaping are not triggered. Thus, the particular use of the descending tectal motor pathways, for attack or for escape, is determined by both tectal and forebrain processing of stimuli.

The spatial mapping of topographically organized projections allows for correct orientation toward prey-sized stimuli and away from threatening stimuli.

THE OPTIC TECTUM IN GROUP II VERTEBRATES

Hagfishes

In the optic tectum of hagfishes, a number of neuron cell bodies are migrated away from the ventricular surface and are scattered throughout most of the thickness of the optic tectum (Fig. 18-18). There is an outer, relatively cell free layer, called a molecular layer, and an inner cell layer, although an extension of the third ventricle into the optic tectum is not present.

The optic tract in hagfishes runs through the brain in a position deeper than in other vertebrates and correspondingly enters the optic tectum from its ventral aspect. Nonetheless, the retinal axons terminate primarily within the more superficial part of the optic tectum. The terminal zone lies in a transition area between the molecular and cell layers. The molecular layer and the area of retinal terminations may thus correspond to the superficial zone of the optic tectum in other vertebrates and the inner cell layer to the central and periventricular zones.

The optic tectum is known to receive afferent projections from the diencephalon, from octavolateral and trigeminal nuclei in the brainstem, and from the dorsal column nuclei. It also receives a spinal projection via the spinal lemniscus, which lies just ventral to it. The spinal lemniscus is in a similar position in lampreys (Fig. 16-1) relative to the optic tectum and terminates sparsely in the ventral part of the optic tectum. Efferent projections of the optic tectum in hagfishes are predominantly to the hindbrain but for the most part remain to be studied.

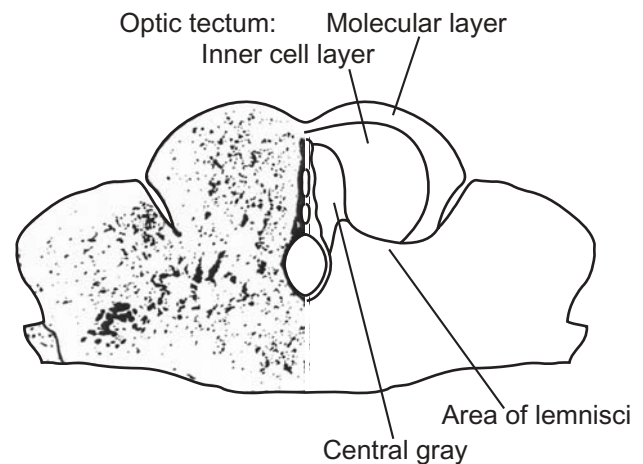


FIGURE 18-18. Transverse hemisection with mirror-image drawing through the left midbrain of a hagfish (*Eptatretus stouti*). Adapted from Ronan and Northcutt (1990) and used with permission of John Wiley & Sons.

Galeomorph Sharks, Skates, and Rays

The optic tectum in cartilaginous fishes with elaborated brains is characterized by cell migration away from the periventricular zone into both the superficial and central zones. The amount of cellular migration is extensive, and the highest density of neuronal cell bodies is in the superficial zone (Fig. 18-19).

The neuronal cell types in the optic tectum consist of a predominance of large, multipolar neurons, which have dendrites radiating in all directions from the cell body (unlabeled, Fig. 18-20). Some neurons with horizontally oriented dendrites are present (Fig. 18-20 a-c), but the small, piriform neurons with radially oriented dendrites, so characteristic of the optic tectum of most other vertebrates, including squalomorph sharks, are conspicuously sparse in number. Pyramidal cells—neurons that have an apical, radially oriented dendrite and two shorter dendrites off the basal part of the cell body—are also sparse to absent. Thus, the anatomical basis for precise, point-to-point topographic input of visual and other information would seem to be missing.

In skates, recordings of electrical activity of neurons in the optic tectum in response to visual stimulation, called evoked potentials, are, however, similar to visually evoked potentials in the optic tecta of other vertebrates, such as frogs and birds, where the small piriform cells are present in abundance. In all these cases, as the recording electrode is lowered through the tectal layers, a reversal of polarity of the signal occurs. The small piriform cells are responsible for this “sink/source” (reversal) phenomenon in other vertebrates. In skates, a set of more migrated cells, which have relatively small cell bodies and dendrites extending both toward and away from the surface of the optic tectum (similar to that in Fig. 18-20 d), have been identified as the population primarily responsible for the “sink/source” distribution of the evoked potentials. One of these cells is shown in Figure 18-21 a, in comparison with sim-

ilarly scaled piriform cells from the optic tecta of a frog (Fig. 18-21 b) and a teleost fish (Fig. 18-21 c). This type of tectal cell in the skate appears to be a migrated version of a piriform cell, with some additional branching of the apical dendrite and the addition of a basal dendrite.

Evolutionary changes in the optic tecta of cartilaginous fishes thus appear to consist of (1) increased migration, accompanied by an increase in neuronal cell density and (2) elaboration of the configuration of the dendritic profiles. Further study of the cells with radially oriented dendrites in skates, in comparison with the piriform tectal cells of other vertebrates, could provide a window onto the evolution of neuronal cell structure.

Afferent projections to the optic tectum arise from the retina and from numerous sites within the brain. Retinal fibers enter the optic tectum deep to its surface and terminate primarily within the superficial zone. The optic tectum receives projections to its central zone from neurons lying in the caudal part of the telencephalon, in a number of nuclei in the diencephalon, and in the contralateral optic tectum. It receives ascending projections from lateral and ventrolateral tegmental nuclei and from the red nucleus. More caudal sites projecting to the optic tectum include vestibular, reticular, trigeminal, and octavolateral nuclei. A cerebellar nucleus and the dorsal part of the cervical spinal cord also project to the optic tectum and terminate in the central zone. Clearly, the optic tectum receives multiple inputs of a feedback nature from structures involved in motor functions in addition to sensory information from multiple systems.

The optic tectum in cartilaginous fishes has three major sets of efferent projections: descending, commissural, and ascending. Descending projections terminate in the reticular formation but do not extend to reach the spinal cord. No connections are present between the optic tectum and a nucleus that has been called nucleus isthmi but whose identity is so far in doubt. Commissural projections terminate in the contralateral optic tectum and also in the intercollicular nucleus, which, like the reticular formation, projects to the spinal cord.

Ascending tectal projections terminate in a number of diencephalic nuclei. Two of these nuclei, which are in the dorsal thalamus, are nucleus anterior and the dorsal posterior nucleus. As in a variety of other vertebrates, nucleus anterior also receives a substantial retinal projection and projects to the telencephalon. The dorsal posterior nucleus does not receive a retinal projection but, like nucleus anterior, projects to the telencephalon. Thus, in cartilaginous fishes, there are at least two major visual pathways (see Fig. 18-14) by which tectal information is relayed to the telencephalon, one of which also has retinal input and one of which does not.

Teleosts

The periventricular, central, and superficial zones in the optic tectum of teleosts are each subdivided into multiple layers of cells and fibers (Fig. 18-22). The layers are clearly demarcated, unlike the more diffuse array of cells seen in the optic tecta of cartilaginous fishes with elaborated brains. Small piriform cells (Fig. 18-23 a and b) with radially oriented dendrites are present in abundance. An unusual population of pyramidal cells (Fig. 18-23 c) is also present. These cells have

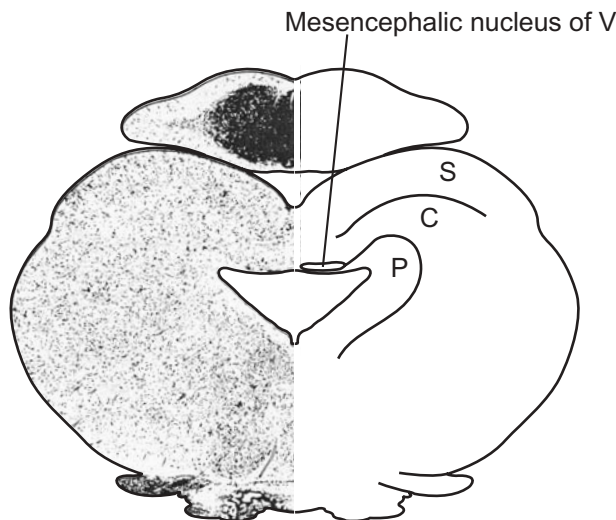


FIGURE 18-19. Transverse hemisection with mirror-image drawing through the left midbrain of a skate (*Raja eglanteria*). Adapted from Boord and Northcutt (1982) and used with permission of John Wiley & Sons.



FIGURE 18-20. Neurons in the optic tectum of a dogfish shark (*Scyliorhinus canicula*) as revealed with the Golgi method. Adapted from Manso and Anadón (1991) and used with permission of John Wiley & Sons.

an extensively branched and spiny apical dendrite and a basal dendrite that branches extensively in the horizontal plane and have not been found in nonteleost vertebrates. Cells with horizontally oriented dendrites and multipolar cells are present, as in the optic tecta of other vertebrates.

A presumably nonneural cell, called a **tanycyte** or **ependymoglia cell**, present in the optic tectum of teleost fishes, should also be mentioned here. These cells are notable for their distinctive morphology, as revealed by the Golgi method and shown in Figure 18-24. The cell body lies in the ependymal layer and has a long apical dendrite, which is studded with a multitude of short processes and extends to the tectal surface. Tanycytes are also found in other locations within the brains of various vertebrates (for example, see Chapter 23).

Afferent fibers from the retina terminate in two layers within the superficial zone of the optic tectum in teleosts. A few fibers also enter and terminate in the deeper part of the

central tectal zone. The retinal projection is topographically mapped, as in other vertebrates. Other tectal afferents arise from nuclei in the telencephalon and diencephalon. The telencephalic afferents arise from neurons within the central zone of the pallium, Dc (see Chapter 25). In the mesencephalon, cells projecting to the optic tectum lie in the contralateral optic tectum, torus semicircularis, nucleus isthmi, and dorsolateral tegmentum and in the ipsilateral torus longitudinalis. Tectal afferents have been reported originating from multiple sites in the more caudal part of the brainstem in teleosts, including the reticular formation, inferior raphe, locus coeruleus, medial octavolateral nucleus, and rostral spinal cord.

The efferent projections of the optic tectum in teleosts are widespread and, in some cases, reciprocal to sites that project to the optic tectum. In the mesencephalon, cells in the tectal hemisphere project to the contralateral optic tectum, dorsolateral tegmentum, and nucleus isthmi. Descending projections have been traced to the mesencephalic reticular formation, and

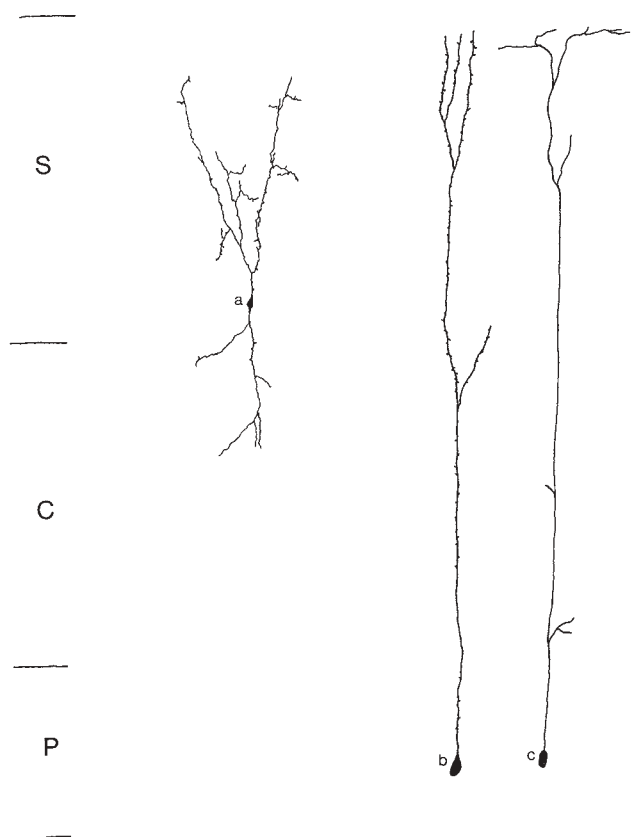


FIGURE 18-21. Comparison of small cell (a) in optic tectum of a skate that has dendrites extending toward both the surface and the periventricular zone with piriform neurons in the optic tectum of a frog (b) and a teleost (c). Data from Witkovsky et al. (1980), Székely (1971), and Vanegas et al. (1974), respectively.

this pathway appears to be involved with the generation of **saccades** (rapid, directed eye movements) for orientation. Axons from the optic tectum that project rostrally to the diencephalon terminate in a number of nuclei, particularly in the pretectum and dorsal thalamus. In the pretectum, a nucleus known as the magnocellular (i.e., “large celled”) superficial pretectal nucleus receives a tectal projection and, in turn, projects to nucleus isthmi, forming an additional relay path for tectoisthmal communication.

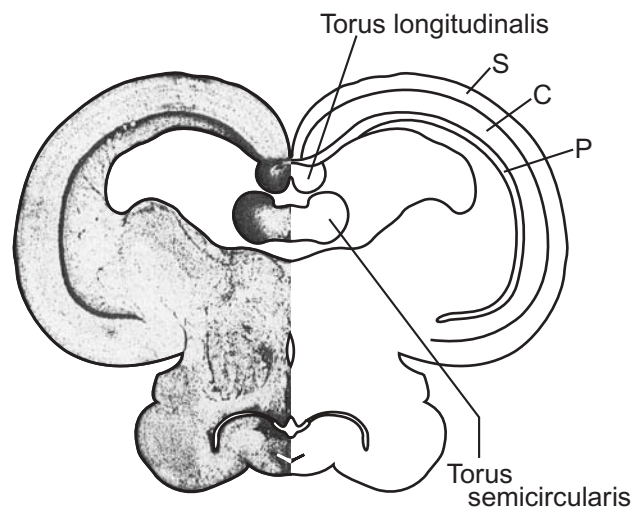


FIGURE 18-22. Drawing of a transverse hemisection with mirror-image outline drawing through the midbrain of a teleost fish (*Lepomis gibbosus*). Adapted from Parent et al. (1978) and used with permission of John Wiley & Sons.

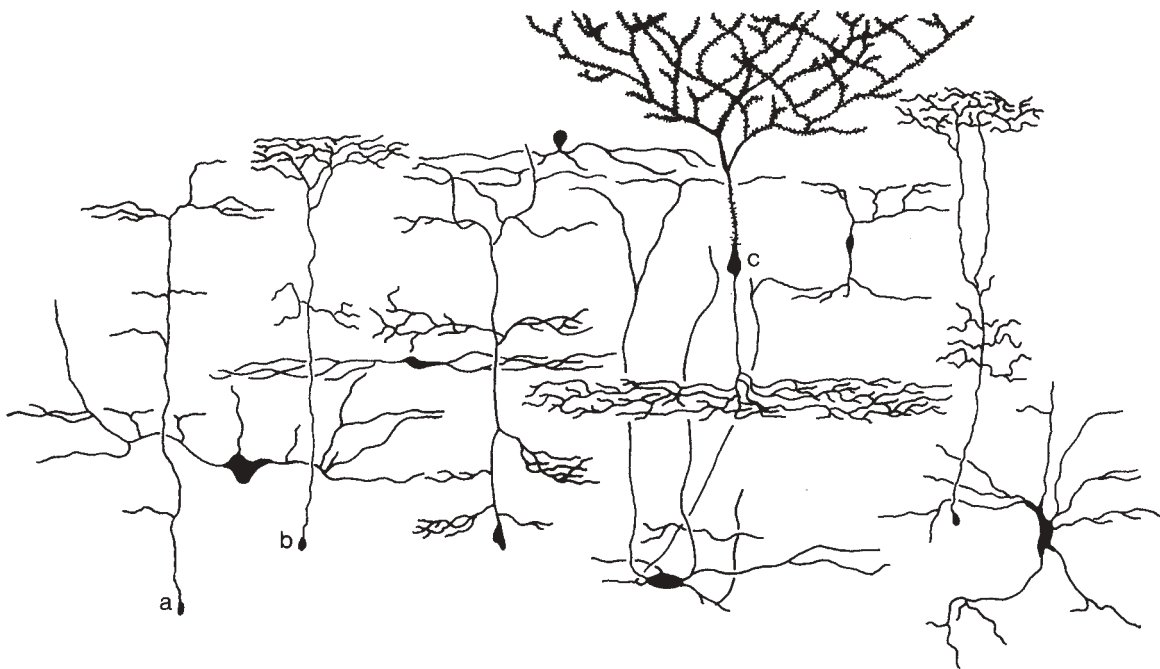


FIGURE 18-23. Neurons in the optic tectum of a teleost (*Eugerres plumieri*) as revealed with the Golgi method. Adapted from Vanegas et al. (1974) and used with permission of John Wiley & Sons.



FIGURE 18-24. A tanyocyte in the optic tectum of a teleost (*Eugerres plumieri*) as revealed with the Golgi method. Adapted from Vanegas et al. (1984) and used with kind permission of Springer Science and Business Media.

In the dorsal thalamus, two nuclei receive tectal projections: nucleus anterior and the dorsal posterior nucleus. Nucleus anterior also receives a substantial retinal projection, while the dorsal posterior nucleus does not. The dorsal posterior nucleus projects to the telencephalon; nucleus anterior also has been found to project to the telencephalon in the goldfish *Carassius auratus* but not in a number of other teleost species. As in the bichir, the optic tectum of teleosts also projects to a nucleus of the posterior tuberculum, which in some taxa has been found to project to part of the pallium of the telencephalon. A visual pathway from the optic tectum to the telencephalon via the posterior tuberculum may thus be a general feature of ray-finned fishes and unique to them.

The tectal connections with nucleus isthmi are reciprocal and topographically organized, as discussed above. The tectal cells that project to nucleus isthmi are a portion of the small piriform cells with radially oriented dendrites that lie in the periventricular gray zone. Topographic mapping of the tectoisthmal and isthmotectal fibers is a common feature in this system in teleosts and tetrapods. In tetrapods, as discussed above for frogs, neurons in nucleus isthmi have relatively small receptive fields, as would be expected from the point-to-point organization of the tectal input. In teleosts, however, neurons in nucleus isthmi respond to small stimuli throughout the visual field. In other words, the receptive fields of individual isthmal neurons are very large.

These large receptive fields of isthmal neurons in teleosts may allow for a role in “alerting” the optic tectum to novel, and therefore important, stimuli that enter any part of the visual field. That such large receptive fields in nucleus isthmi are present is an unexpected finding, however, in light of the topographic tectal input from the small piriform cells. Possible

explanations for this phenomenon include branching and overlapping terminal areas of tectal axons onto isthmal neurons, a possibly nontopographic input from the magnocellular superficial pretectal nucleus, or electrical coupling among isthmal neurons (achieved through very close junctions, called tight junctions, between cell bodies).

The tectum also receives an input from the torus longitudinalis (Fig. 18-22), a cerebelloid structure (see Chapter 14) unique to ray-finned fishes. This structure comprises a pair of ridges that extend rostrocaudally along the medial aspect of the tectum and is involved in visuomotor functions. It receives projections from several sources, mainly from two nuclei that lie in the hindbrain ventral to the cerebellum—the nuclei subvalvularis and subeminentialis pars magnocellularis—and other neurons that lie along a fiber tract in the same region. Other afferent sources include the nucleus paracommissuralis in the pretectal region, the optic tectum itself, and the torus semicircularis. Nucleus paracommissuralis appears to relay telencephalic inputs from the central part of the pallium (Dc; see Chapter 25) to both the torus longitudinalis and the cerebellum.

The torus longitudinalis gives rise to axons that run in the marginal layer (stratum marginale) on the outer surface of the optic tectum and that synapse, in topographic order, on the distal dendrites of pyramidal tectal neurons, such as that shown in Figure 18-23 c. These pyramidal neurons also receive retinal projections, and both the retinal and toral synapses on the pyramidal neurons are excitatory. The toral fibers synapse on a more distal part of the dendritic tree of the pyramidal cell than do the retinal fibers, so the toral input can activate the dendritic tree, making it more receptive to visual input. A proposed circuit involves projections from the pyramidal cells to other tectal neurons located deeper, in the central zone, which in turn project back to the torus longitudinalis. The resulting closed circuit would then play a role in regulating the influence of descending visual input on the motor output functions of both the optic tectum and the cerebellum.

Amniotes

In mammals, the optic tectum, which is often called the superior colliculus, is generally less impressive in size, relative to other brain structures, than in most other vertebrates. Among mammals, this structure is best developed in those with arboreal or partly arboreal habitats, such as squirrels, tree shrews, and some primates. The superior colliculus is laminated in mammals and can be divided into superficial, intermediate (central), and periventricular zones. These three zones can be subdivided into eight layers. As shown in Figure 18-25, the superficial zone is divided into the **stratum zonale** (SZ), the **stratum griseum superficiale** (SGS), and the **stratum opticum** (SO). The bulk of the retinal fibers projecting to the superior colliculus pass through the latter. The central zone is divided into the **stratum griseum intermediale** (SGI) and the **stratum album intermediale** (SAI), while the deep zone comprises the **stratum griseum profundum** (SGP), the **stratum album profundum** (SAP), and the **central gray** (CG). When the “deep layers” of the superior colliculus are referred to, only the SGI and SAI are usually meant. The central gray is usually referred to separately and is alternatively called the **periaqueductal gray**, or PAG. An often overlooked feature

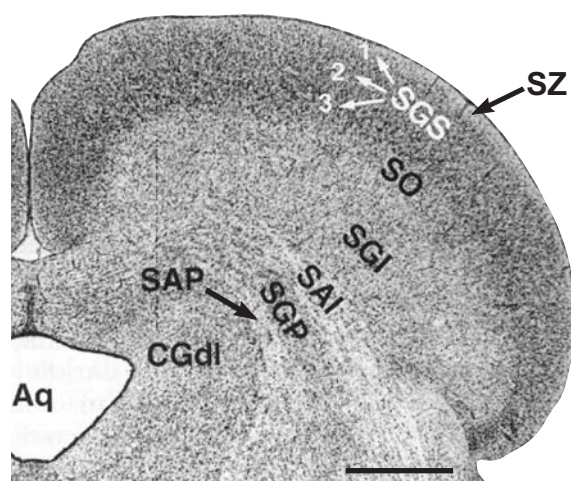


FIGURE 18-25. Transverse hemisection through the right superior colliculus of a ground squirrel stained for Nissl substance. Abbreviations (from superficial to deep): SZ, stratum zonale; SGS, stratum griseum superficiale (also known as the stratum cinereum); SO, stratum opticum; SGI, stratum griseum intermediale; SAI, stratum album intermediale; SGP, stratum griseum profundum; SAP, stratum album profundum; CGdl, dorsolateral part of central gray; Aq, cerebral aqueduct. From Major et al. (2000) and used with permission of John Wiley & Sons.

of the mammalian tectum is the relative enlargement of its periventricular zone, particularly of the central gray. Within the various tectal layers, piriform neurons with radially oriented dendrites and a variety of horizontally oriented and larger, multipolar cells are present (Fig. 18-26).

Afferent fibers from the retina terminate topographically in the superficial zone (SGS) of the superior colliculus—the majority in the outermost of its three sublayers, SGS1, and others in its middle layer, SGS2. In mammals, three physiologically different types of retinal ganglion cells have been identified and are referred to as X (or P), Y (or M), and W (or K) cells (see Chapter 26). Although all three types project to visual targets in the diencephalon, only the Y and W retinal ganglion cells project to the superior colliculus. The W cells in particular project substantially to SGS1. Other afferent projections arise in parts of the visual cortex in the pallium of the telencephalon and terminate in the superficial zone. Likewise, some diencephalic projections and those from the mammalian homologue of nucleus isthmi, the parabigeminal nucleus, terminate in the superficial zone.

Telencephalic cortical areas, including somatosensory and visual cortices as well as a more rostral part of cortex involved in eye movements, also project to the central and periventricular zones of the superior colliculus, as do fibers from the posterior pretectal nucleus and from the substantia nigra that relay telencephalic striatopallidal input to the superior colliculus. The spinal (descending) trigeminal nucleus projects to the deeper zones of the superior colliculus, providing topographic representation of somatosensory input from the face. Other sources of afferent input include nuclei in the hypothalamus and thalamus, the contralateral superior colliculus, the reticu-

lar formation, the spinal cord, and a variety of other brainstem sites.

Efferent projections can be divided into ascending, commissural, and descending pathways, as in other vertebrates. The major ascending pathway from the superior colliculus to the dorsal thalamus arises from neurons whose cell bodies lie predominantly in the deepest of the three SGS sublayers, SGS3, and terminates in nuclei that are collectively called the **lateral posterior—pulvinar** (or **LP/pulvinar**) complex, which in turn project to visual pallial areas in the telencephalon. A second tectal pathway to the dorsal thalamus terminates in nuclei of the **posterior nuclear group**. The cells of origin of this pathway lie in multiple layers, most in the SGI but some also in deeper as well as in the more superficial tectal layers, SO and SGS3. These posterior thalamic nuclei also project to the telencephalon, both to extrastriate visual cortical areas and to part of the amygdala. A minor tectothalamic projection is present to the **dorsal lateral geniculate nucleus**, which also receives direct and substantial retinal projections and projects to visual pallium.

The connections of the superior colliculus with the contralateral superior colliculus and with the parabigeminal nucleus are topographic and reciprocal. Descending tectal fibers project to numerous sites, including the reticular formation, motor relay nuclei in the pons, and the spinal cord.

The superior colliculus plays an important role in visuomotor behavior in mammals, as it does in other vertebrates. The superior colliculus is involved in orienting to visual stimuli by head movements and/or saccades. Tectal neurons respond to features of stimuli that include location, movement, brightness, and pattern. Deficits in the ability to notice and to then pay attention to objects in the visual field occur when the superior colliculus is damaged.

In cats and other mammals that use both head and body movements as well as saccadic eye movements to orient to a stimulus, the superior colliculus functions in all these behaviors, as it does in nonmammalian vertebrates. In primates, the primary response to an object of interest in the peripheral part of the visual field is to move the eyes, in preference to or before moving the head or body. The saccade is made in order to bring the object into the central visual field, where acuity is greatest. One of the primary roles of the superior colliculus in primates is in initiating and controlling the motor sequence for saccades.

The superior colliculus in primates also plays a key role in visual attention. A clinical case study in a human with damage to the major dorsal thalamic tectal target, the pulvinar, revealed neglect of stimuli in the peripheral part of the visual field. The degree of neglect was dependent on how far peripherally the stimulus was presented, the size and brightness of the stimulus, and the length of presentation of the stimulus. In the trials in which saccadic eye movements were made to the stimulus, the latency (interval between stimulus presentation and response) was abnormally long, and spontaneous eye movements were observed to be fewer than normal.

The superior colliculus also plays a significant role in predation. The degree to which the tectospinal tract is developed in mammals is directly correlated with the degree of predation in given species. This differential development of the tract has occurred independently at least four times within mammals.



FIGURE 18-26. Some of the types of neurons present in the optic tectum of a mammal as revealed with the Golgi method. Data from Ariëns Kappers et al. (1967) as redrawn from Ramón y Cajal.

A highly unusual exception to the dominance of visual processing by the superior colliculus occurs in the star-nosed mole (Fig. 18-27). This mammal has an entirely fossorial (subterranean) habitat. Its visual system is markedly reduced, but it has an elaborately specialized tactile system of 11 pairs of fleshy appendages that encircle the snout (see Chapter 2). These appendages send a major input to the superior colliculus via the trigeminal system, and the mole is able to make frequent and precise orienting movements to novel stimuli by utilizing this system. A tactile fovea on appendage 11 is moved in a saccade-like manner while the mole explores its environment. The superior colliculus shows reduction of the more superfi-

cial layers, but all layers contain cells responsive to tactile stimuli, and the representation of the fleshy appendages on the contralateral tectum is very large, in proportion to the high density of somatosensory receptors on the appendages.

The optic tectum in reptiles is characterized by numerous cellular laminae that are distributed across the superficial, central, and periventricular gray zones. In some reptiles, such as turtles (Fig. 18-28), the lamination is moderately demarcated, but in some lizards (Fig. 18-29), the lamination is particularly well pronounced. In all reptiles, most of the tectal layers and zones are arranged like those in mammals. The only significant exception is that the stratum opticum (SO), in which the affer-

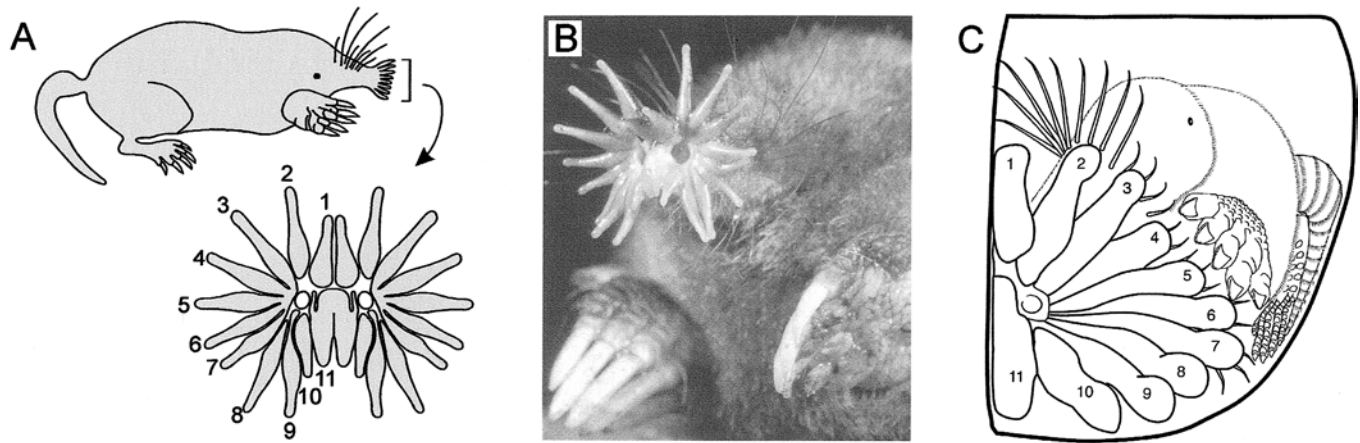


FIGURE 18-27. The unique sensory receptor adaptation of the star-nosed mole and its projection onto the superior colliculus. A: Drawing of the star-nosed mole (*Condylura cristata*) and the ring of 22 fleshy appendages that ring the snout. B: Photograph of the snout region showing the snout ring of fleshy appendages. C: Schematized representation of the fleshy appendages and other somatosensory inputs on the contralateral superior colliculus. Rostral is toward the bottom and medial toward the left. From Crish et al. (2003) and used with permission of John Wiley & Sons.

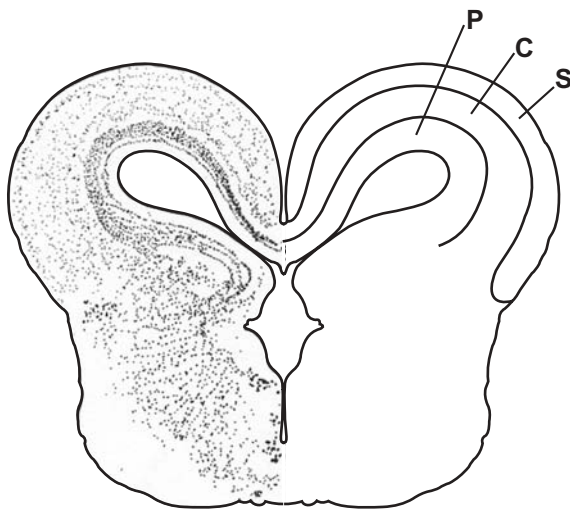


FIGURE 18-28. Transverse hemisection with mirror-image drawing through the midbrain in a turtle (*Chrysemys scripta elegans*). Adapted from Browner et al. (1981) and used with permission of John Wiley & Sons.

ent retinal fibers lie, occupies the most superficial part of the optic tectum, rather than the deeper part of the superficial zone as in mammals. As shown in Figure 18-29, a total of 14 layers (or strata) can be recognized. By convention, the layers are numbered consecutively from the deepest to the most superficial. An abundance of small piriform cells, with long, radially oriented dendrites (Fig. 18-30 a-h), small cells with more complexly branched dendritic trees (Fig. 18-30 i-k), small horizontally oriented cells (Fig. 18-30 l-p), and large multipolar cells (Fig. 18-30 q-s) are present. It should be noted that,

while comparable zones can be consistently recognized across all amniotes, some specific cell populations might migrate to a greater or lesser degree. As discussed below, the tectum gives rise to a minor projection to the dorsal lateral geniculate nucleus in all amniotes. In turtles, the tectal neuron somas that give rise to this projection lie within the periventricular zone, while the homologous population of neuron somas in mammals lies within the superficial zone.

Retinal fibers terminate topographically in the superficial zone (layers 8–13). Somatosensory input from the dorsal spinal cord and dorsal column nuclei terminates in the central tectal zone in spatially mapped register with the visual map. In snakes that have IR-detecting pit organs, IR input is relayed through a brainstem trigeminal nucleus to a nucleus, nucleus reticularis caloris, which lies in the medulla, and thence to the optic tectum. The map of IR input is partly distorted, with the area of the central, frontal field magnified on the optic tectum, relative to the visual map. Several regions in the tegmentum proper, nucleus isthmi, and a number of nuclei in the diencephalon and pretectum also project to the optic tectum.

There are several pathways from the telencephalon to the optic tectum in reptiles. The visual pallium projects directly to the optic tectum. Additionally, the dorsal pallidum (globus pallidus) in the telencephalon receives input from the dorsal striatum and projects to the optic tectum via two relays: a nucleus in the pretectum, called the **dorsal nucleus of the posterior commissure**, and the **substantia nigra pars reticulata** in the midbrain tegmentum. The dorsal striatopallidum (see Chapter 24) is involved in the control of movements. These relayed inputs to the optic tectum thus modulate the orienting and other movements directed by the optic tectum in response to localized sensory stimuli.

Efferent projections of the optic tectum in reptiles include those descending to terminate in nucleus isthmi, parts of the

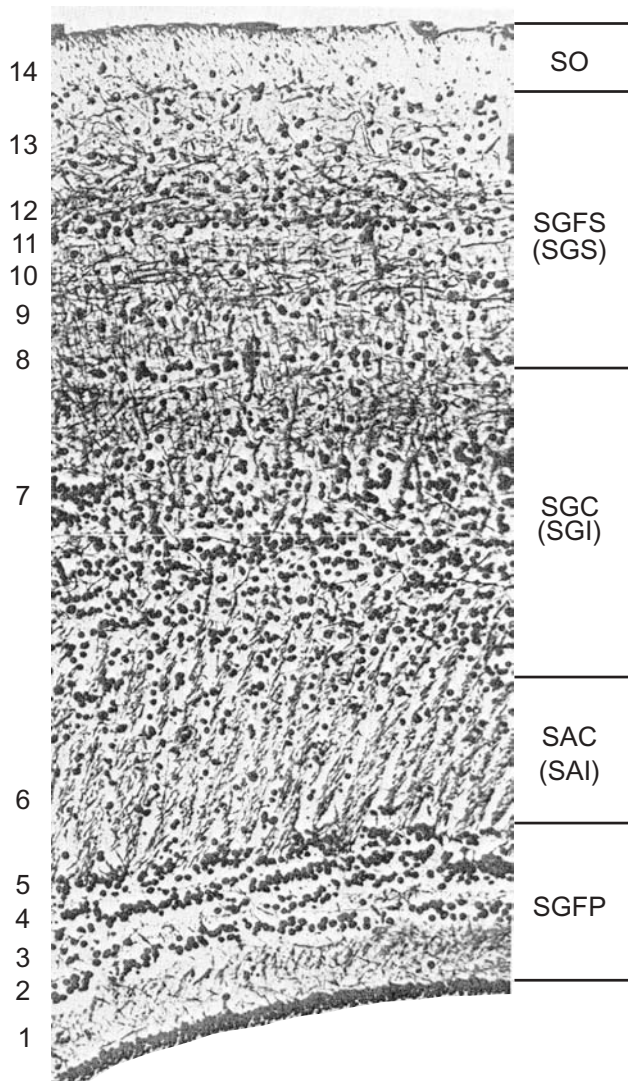


FIGURE 18-29. Portion of a transverse hemisection through the optic tectum of a lizard (*Iguana iguana*). Abbreviations: SO, stratum opticum; SGFS, stratum griseum et fibrosum superficiale; SGC, stratum griseum centrale; SAC, stratum album centrale; SGFP, stratum griseum et fibrosum periventriculare. The mammalian-equivalent terminology is indicated by the abbreviations in parentheses: (SGS), stratum griseum superficiale; (SGI), stratum griseum intermediale; (SAI), stratum album intermediale. Numbers indicate layers 1–14. Adapted from Northcutt (1984) and used with kind permission of Springer Science and Business Media.

tegmen, the reticular formation, and the rostral spinal cord. These projections allow for the motor programs of orienting to stimuli, capturing prey, and escaping predators. The optic tectum also projects to the contralateral optic tectum and to nuclei in the pretectum and dorsal thalamus.

In the dorsal thalamus, the nucleus that receives most of the tectal projections is **nucleus rotundus**, a large, round nucleus that, in turn, projects to the telencephalon. This pathway is one of the two major visual pathways to the telencephalon. It originates from neuron somas located in the

deeper part of the superior colliculus, the SGC (Fig. 18-29). The primary site of termination for this pathway through nucleus rotundus is within the pallium—not in the dorsal striatum as is the case in amphibians. The other visual pathway to the telencephalon consists of both a minor tectal projection and a substantial retinal projection to a nucleus called the **dorsal lateral geniculate nucleus** (the homologue of the dorsal lateral geniculate nucleus of mammals) that, in turn, also projects to the pallium.

The layering of the optic tectum in birds is even more crisply demarcated than it is in reptiles, although its populations of horizontal cells, large, multipolar cells, an abundance of small piriform cells, and other elements are similar. Fifteen layers of the optic tectum are generally recognized in birds (Fig. 18-31 and see Fig. 17-16). The “extra” layer is due to the fact that seven individual layers are recognized as layers 2–8, while in lizards, for example, only six recognized layers (8–13) constitute the same part of the tectum.

By convention, the layers of the avian tectum are numbered from superficial to deep, which is the opposite of the convention in reptiles. Thus, in birds the most superficial tectal layer is layer 1, and the deepest layer, which borders the tectal ventricle, is layer 15. Note that the latter layer is not included in the photomicrograph in Figure 18-31.

In comparing the avian tectum with the tectum in reptiles, a disparity exists in the placement of the boundary between the superficial and central zones. In Figure 18-31, the iguana tectum is shown on the left for comparison with the pigeon tectum on the right. The deep boundary of the superficial zone (SGFS) of the lizard tectum is placed between its layers 7 and 8. Even though the numbering systems go in opposite directions, the densely packed line of cell somas in layer 8 of the avian tectum clearly corresponds to somewhat less dense but comparably thin layer 8 of the lizard tectum. The superficial zone as defined in the lizard tectum would thus end here in birds as well, as indicated by the shaded SGFS zone shown in the center of the figure, and these superficial layers in all reptiles and birds are the ones that receive the direct retinal fiber terminations. However, the superficial zone as defined in birds (and sometimes turtles) includes the avian layers 9–12 as well and thus extends down to the border between layers 12 and 13, as indicated by the shaded SGFS zone shown at the far right of the figure. Only layer 13 is designated as the central zone (SGC) in birds. The details of this mismatch are not crucial to our purposes here but are noted to avoid confusion. Just as brains evolve, terminology evolves, and future selective pressures against this terminological disparity eventually will result in its correction in the literature.

In addition to the retinal afferent terminations within the avian tectum, specifically in layers 2, 3, 4, 5b, and 7, somatosensory and other inputs terminate solely or predominantly in the tectal layers deep to layer 8. These afferent projections include input relayed from the dorsal striatum in the telencephalon through **nucleus spiriformis lateralis** (the homologue of the dorsal nucleus of the posterior commissure of reptiles) and probably that through the substantia nigra pars reticulata as well. Part of the visual pallium in the telencephalon also projects directly to the optic tectum, and these fibers predominantly terminate in layers 11–13. Additional tectal afferents arise in tegmental and other caudal areas, three

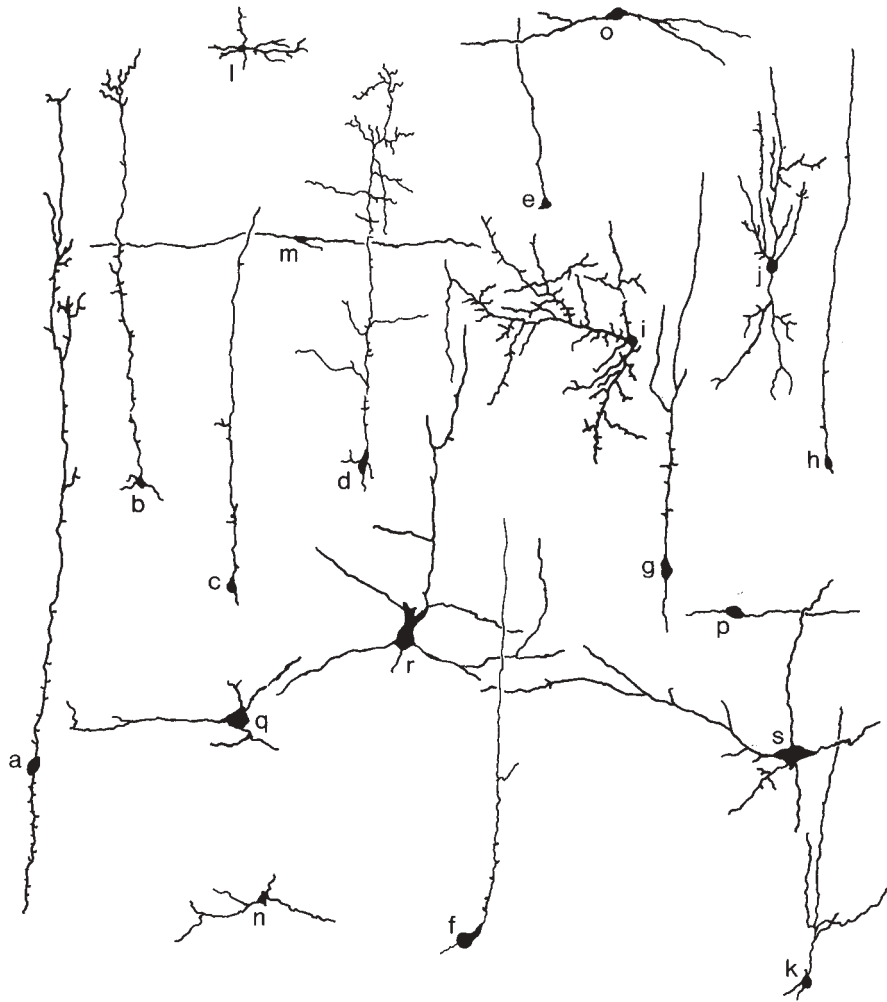


FIGURE 18-30. Neurons in the optic tectum of a lizard (*Tupinambis nigropunctatus*) as revealed with the Golgi method. Adapted from Butler and Ebesson (1975) and used with permission of John Wiley & Sons.

isthmal nuclei (nuclei isthmi, pars parvocellularis and pars magnocellularis, and nucleus semilunaris), and thalamic and pretectal nuclei, as they do in reptiles.

Tectal efferent projections in birds are similar to those in reptiles. Ascending projections terminate in a number of dorsal thalamic and pretectal nuclei, including nucleus rotundus. The latter nucleus projects to part of the pallium in the telencephalon, the entopallium, forming one of the two major ascending visual pathways. The second major visual pathway to the telencephalon is relayed through a separate dorsal thalamic nucleus, the dorsal lateral geniculate nucleus. As in other amniotes, the tectum in birds contributes a minor projection to this nucleus. In birds, the optic tectum and the ascending tectofugal system via nucleus rotundus have been found to play an important role in visual discrimination tasks—distinguishing one pattern from another or the relative degree of brightness or colors—as well as in localizing stimuli in visual or somatosensory space. The tectal neurons that project to

nucleus rotundus lie in layer 13, conventionally designated the central gray layer (SGC). These neurons are called tectal ganglion cells, and the terminal endings of their dendrites have a unique and striking morphology such that they are called bottlebrush endings. This morphological fingerprint has also been identified in an apparently homologous population of tectothalamic neurons in mammals (see Box 18-2).

Other tectal connections in birds include commissural projections to the contralateral optic tectum, reciprocal projections to the parvocellular, magnocellular, and semilunar isthmal nuclei, and a projection to the neighboring isthmo-optic nucleus that, in turn, projects to the retina. Descending projections of the optic tectum do not extend to the spinal cord directly, as they do in many other vertebrates, but terminate in areas in the brainstem tegmentum and the reticular formation, which, in turn, project to the spinal cord. These pathways serve motor functions for orienting to localized stimuli with rapid head movements.

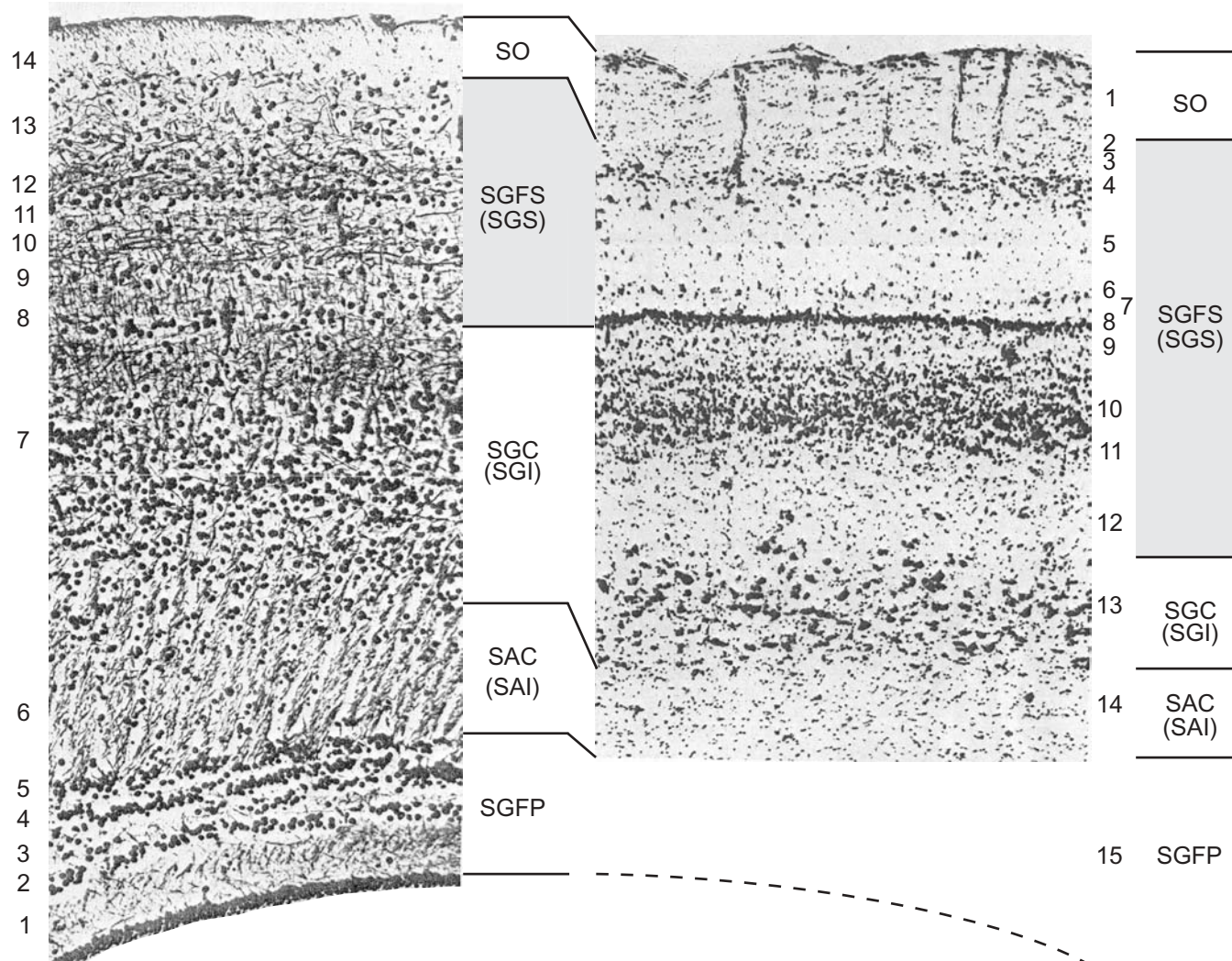


FIGURE 18-31. Portion of a transverse hemisection through most of the thickness of the optic tectum in the pigeon (*Columba livia*), stained for Nissl, on the right, compared with the entire thickness of the optic tectum in an iguana (from Fig. 18-29) on the left. The numbers to the right indicate all 15 of the avian tectal layers. The deepest layer, layer 15 (the periventricular gray and white layer), is not included in the photomicrograph. The numbers to the left indicate the full total of 14 tectal layers of the iguana tectum. Abbreviations (used for both bird and lizard): SO, stratum opticum; SGFS, stratum griseum et fibrosum superficiale; SGC, stratum griseum centrale; SAC, stratum album centrale, and as shown for the lizard tectum, SGFP, stratum griseum et fibrosum periventriculare. The mammalian-equivalent terminology is indicated by the abbreviations in parentheses: (SGS), stratum griseum superficiale; (SGI), stratum griseum intermediale; (SAI), stratum album intermediale. The letter-abbreviated zone designations in the center of the figure indicate the standard zones that are recognized in the iguana tectum and the zonal divisions that would correspond to those in the avian tectum. In contrast, the zonal divisions that are in common usage for the avian tectum are shown to the far right, resulting in a disparity of terminology. Only the external part of the SGFS (the SGFe, not specifically labeled in figure) of the avian tectum (its layers 2–8), corresponds to the superficial zone of the lizard tectum (its layers 8–13). The internal part of the SGFS (the SGFi) of the avian tectum (its layers 9–12) plus its layer 13 (designated SGC) together correspond to the central zone of the lizard tectum. The Nissl photomicrograph of lizard tectum is from Northcutt (1984) and that of pigeon optic tectum from Hunt and Brecha (1984). Both portions of this figure are used with kind permission of Springer Science and Business Media.

BOX 18-2. Tectal Ganglion Cells With Bottlebrush Dendritic Endings: Questions About Tectal Lamination

Harvey Karten and his co-workers recently have described several populations of tectal neurons in both birds and mammals. These cells are called tectal ganglion cells (TGCs), and they are characterized by a heavily arborized terminal part of their dendrites that resembles a bottlebrush in configuration. The location of their cell bodies within the tectal laminae appears to be different between birds and mammals, however, with the cell somas lying in the superficial zone in mammals (SGS) but in layer 13 in birds, designated as the SGC. As noted below, even though many laminar features of tectal organization are constant across vertebrates, this apparent difference in laminar position of the TGCs may not be of significance in regard to the homology of the populations between birds and mammals.

Pigeons have at least five types of tectal ganglion cells, two of which also have been found in chicks and will be focused on here. The type I tectal ganglion cells [Fig. 1(A)] have substantial bottlebrush dendritic endings, and these endings lie within tectal layer 5a, which receives a direct retinal input. The latter is from small retinal ganglion cells. The cell somas of these cells lie in the more superficial part of layer 13, and they project to two divisions of nucleus rotundus in the dorsal thalamus—its anterior (Ra) and central (Rc) parts. In contrast, the dendritic endings of the type II tectal ganglion cells are more variable, only some having the bottlebrush configuration, and all their endings lie deep to the layers of direct retinal input (in layers 8 and 9). The cell somas of these cells lie in the deeper part of layer 13, and they project to two other divisions of nucleus rotundus—its posterior (Rp) and triangularis (Rt) parts. In summary, type I TGCs have bottlebrush endings with direct retinal input, have cell somas in the superficial part of layer 13, and project to Ra and Rc. Only some of the type II TGCs have bottlebrush endings, and all of them lack direct retinal input, have cell somas in the deep part of layer 13, and project to Rp and Rt.

Similar TGCs have been described in a lizard and a frog, and while not definitively identified due to technical differences that limited the filling of distal dendrites, such cells probably are present also in turtles. Margarita Belekova and her colleagues recently found cells in the turtle tectum that have several characteristic features of TGCs. These cells, which project to nucleus rotundus, have their somas in the central zone (SGC) and dendritic ramifications in the directly retinorecipient superficial zone. Interestingly, as discussed further below, the tectothalamic neurons vary in size and shape, allowing the possibility that they comprise more than one population.

In mammals, two similar populations of TGCs have been identified, although the better case for similarity has been made to date for the type I. These neurons [Fig. 1(B)] have cell somas that lie within the deepest of three strata of the superficial gray zone, referred to as SGS3, and they have

bottlebrush dendritic endings that ramify in the directly retinorecipient layer, SGS1. The type II TGCs of mammals have cell somas that lie slightly deeper in the stratum opticum (SO). Their bottlebrush dendritic endings are mostly restricted to the second stratum of the superficial gray zone, called SGS2, which receives only a minor retinal input at best. Just as in birds, the type I and type II TGCs of mammals may project to different parts of the tectorecipient dorsal thalamus, particularly the lateralis posterior/pulvinar (LP/pulvinar) complex of nuclei. Thus, like the situation in birds, the type I TGCs have somas located superficial to those of the type II TGCs; the type I TGCs receive a major direct retinal input, whereas the type II TGCs do not; and the two types of TGCs project to different parts of the tectorecipient dorsal thalamus.

While similarities in dendritic morphology, inputs, and projection patterns of the TGC populations in birds and mammals are thus striking, there remains the apparent difference in the location of their cell somas within the tectal layers. Both populations of TGCs in birds lie in what has been regarded as the deep part of the central zone of the tectum, while in mammals, both populations clearly lie in the superficial zone. One possibility is that layers 1–13 of

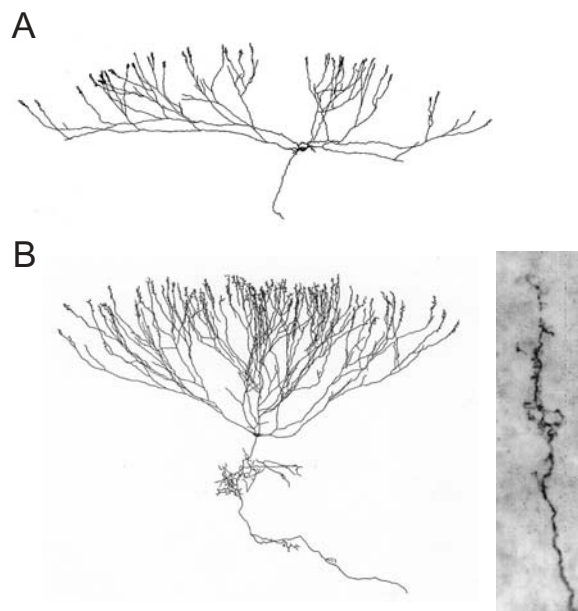


FIGURE 1. Drawings of tectal ganglion cells with bottlebrush dendritic endings in pigeon (A) and mammal (B), with a photomicrograph of a single dendrite of the latter cell with its bottlebrush dendritic endings shown to the right. After Luksch et al. (1998) and Major et al. (2000), respectively. All parts of this figure used with permission of John Wiley & Sons.

BOX 18-2. Tectal Ganglion Cells With Bottlebrush Dendritic Endings: Questions About Tectal Lamination—cont'd

the bird tectum are homologous only to the superficial zone of the mammalian tectum, with layer 14 being homologous to the stratum opticum of mammals. This would leave only the deepest layer of the tectum, layer 15, as a candidate for homology with the intermediate (central) and deep zones of the mammalian tectum. However, the possible comparison of layers 1–13 to the superficial zone of mammals is not supported by other findings of connections and comparative cytoarchitecture for layers 9–13 across vertebrates, including the origin of descending tectal projections and the position of mesencephalic V cells (see Chapter 11).

A different possibility is that specific populations of neurons migrate to a variable degree in different taxa. This argument is cogently made by Anton Reiner. He compared the relative position of tectorotundal (and in mammals tecto-LP/pulvinar) neurons across tetrapods, noting that in frogs and mammals the cell somas for this projection lie in the superficial zone, whereas in birds and reptiles they lie in the central zone. A striking finding is that the cell bodies for the tectal projection to the dorsal lateral geniculate nucleus likewise show the same differences in laminar position. In frogs and mammals, these neuron cell bodies lie in the superficial zone of the tectum, while in birds and reptiles, they lie in the central zone. (In birds, these cells lie in what has been called the deep part of the superficial zone, as discussed in the text, but in a lamina that corresponds to the central zone of reptiles, amphibians, and fishes.) In turtles, they lie in the periventricular gray layer. Because it is well established that these tectogeniculate cell populations in different tetrapod taxa are homologous, it is clear that variation in laminar position can occur between such populations.

One of the reasons why the identity and homology of the various populations of tectothalamic neurons is important concerns the two tectothalamic pathways in mammals—one to LP/pulvinar, which is then relayed predominantly to extrastriate cortical areas and the other to nuclei of the posterior nuclear group, which is then relayed predominantly to the lateral nucleus of the amygdala. Until recently, the tectal neurons that are the origin of the posterior group pathway were thought to lie in the intermediate (central) zone of the mammalian tectum. Thus, by laminar position, the TGCs with bottlebrush endings in birds would correspond to these tectoposterior neurons of mammals rather than to the tecto-LP/pulvinar neurons. In fact, identifying a population of tectal neurons in birds and/or reptiles that is comparable to the posterior group-projecting cells in mammals is one of several crucial missing parts of the puzzle needed to resolve the homology of major components of the telencephalon, the ultimate site of the ascending tectal visual pathway.

Recent studies in mammals have demonstrated that projections to the posterior nuclear group arise from

neurons with their cell somas in a wide range of layers within the superior colliculus. The projections to one of these nuclei [called the suprageniculalte nucleus (Sg)] arise from cell somas in the superficial zone, most within the stratum opticum but a few even more superficially in SGS3. Additionally, cell somas in the intermediate (central) and deep (SGP) layers also project to Sg as well as to the rest of the posterior nuclei. Thus, on laminar grounds alone, one cannot argue for homology of the various populations of tectothalamic neurons. Further, these tectoposterior neurons have quite a range of morphology, including stellate, vertical, granular, triangular, and horizontal cell types. One wonders whether some of the type II TGC neurons in birds—those without the bottlebrush dendritic endings—or other tectothalamic projecting populations might be homologous to these tectoposterior neurons in mammals. In birds, the type II TGCs project to the posterior and triangular divisions of nucleus rotundus, which are arguably similar on topographic grounds to the posterior group nuclei of mammals.

It is clear that, in mammals, multiple pathways transmit tectal visual and multisensory information to the thalamus and thence to the telencephalic pallium—whether to cortical and/or amygdalar sites. Identification of similar multiple pathways in birds and reptiles will do much to clarify the relationship of nucleus rotundus and its divisions to the LP/pulvinar and/or posterior nuclear group formations in mammals and to likewise clarify the relationship of the telencephalic target of nucleus rotundus, the visual part of the anterior dorsal ventricular ridge (entopallium in birds), to the cortical areas and/or lateral amygdala of mammals.

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BOX 18-2. Tectal Ganglion Cells With Bottlebrush Dendritic Endings: Questions About Tectal Lamination—cont'd

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EVOLUTIONARY PERSPECTIVE

The optic tectum is one of the most conservative structures in the brains of vertebrates. Although the optic tectum varies in the extent of its development in different vertebrate classes, its layered structure, its cell types, and its afferent and efferent connections are quite similar in all vertebrates. Many of its connections are topographic; this feature is basic for tectal function in localizing stimuli and responding to them in spatially appropriate ways. In spite of this conservative pattern, some significant differences have occurred in the structure and connections of the optic tectum in certain vertebrate radiations.

The migration of neurons into the central and superficial zones of the optic tectum has occurred independently in all four of the major radiations of vertebrates, and the degree of migration of some specific populations of neurons varies across and even within groups. Other specializations have evolved independently as well, in the types of tectal neurons present, in connections of the optic tectum, and in the presence of some structures associated with the optic tectum.

The presence of small piriform neurons with radially oriented dendrites is a common feature of tectal organization except in Group II cartilaginous fishes, the galeomorph sharks, skates, and rays. In these animals, small piriform cells are conspicuously absent; instead, one finds a population of cells with a more elaborate dendritic profile that may be a migrated, elaborated form of piriform cell.

In teleosts (the Group II ray-finned fishes) piriform, horizontal, and multipolar tectal neurons are present as in other vertebrates. Additionally, a population of neurons with extensively branched and spiny apical dendrites and extensively branched, horizontally extending basal dendrites is present. This population of branched, spiny neurons appears to be unique to teleosts.

The presence of such unique neurons in teleosts and the presence of the migrated variant of piriform cells in Group II cartilaginous fishes suggest specializations of tectal function in

these two groups. These specializations have been evolved independently of each other, as neither of these cell types is present in any Group I vertebrate, including the nonteleost ray-finned fishes and the squalomorph sharks.

Variation also occurs in connections and in structures associated with the optic tectum. For example, a nucleus isthmi, which is reciprocally connected with the optic tectum, has been found in both Groups I and II of the ray-finned fishes and in all tetrapods as well: the Group I amphibians and the Group II amniotes. Such a nucleus has not been found in any of the cartilaginous fishes or in lampreys or hagfishes. This structure may thus be a specialization (apomorphy) unique to ray-finned fishes and tetrapods. Completely unique to ray-finned fishes may be the visual pathway from the optic tectum to the telencephalic pallium via a nucleus that lies within the posterior tuberculum. Such a pathway has not been identified in any other group of vertebrates.

A second structure associated with the optic tectum, which is present in both Groups I and II of ray-finned fishes, is the torus longitudinalis, which receives relayed information from the telencephalon and projects to the optic tectum. A torus longitudinalis is not present in any tetrapod or in the outgroups to ray-finned fishes, the cartilaginous fishes and agnathans. Thus, it is an apomorphy in ray-finned fishes that was probably absent in the common ancestral group of the ray-finned fishes and the sarcopterygians.

Variation related to afferent tectal input from the telencephalon is present. Further study to clarify the situation is needed as a number of the studies in nonamniote vertebrates have involved large telencephalic lesions or large applications of axon tracers and have not revealed the specific location(s) of origin of tectally projecting neurons within the telencephalon. Recent work in a teleost fish demonstrated tectal projections arising from the relatively large cells within the central zone of the pallium, an area that appears to be a common output center for the various pallial areas.

In amniotes, the striatum projects via two relay nuclei to the optic tectum, thus providing information on motor control systems. One of these nuclei is the dorsal nucleus of the pos-

terior commissure of reptiles (nucleus spiriformis lateralis of birds and posterior pretectal nucleus of mammals) and the other is the substantia nigra pars reticulata. Of these two pathways, the one through the dorsal nucleus of the posterior commissure is developed better in nonmammalian amniotes, while the one through the substantia nigra is developed better in mammals. Additionally, in mammals, several parts of the neocortex project directly to the optic tectum, providing feedback information; in reptiles and birds, the visual pallium in the telencephalon likewise projects to the optic tectum.

Salamanders have a direct telencephalotectal pathway, whereas in frogs, only a telencephalic projection to the optic tectum via a thalamic relay nucleus has been identified. Both Group I and Group II teleosts have a direct telencephalotectal pathway, as do Group II cartilaginous fishes. Information is not available for Group I cartilaginous fishes or for any agnathans.

If direct telencephalotectal projections arise in the visual pallium rather than the striatum in all cases, and if such projections are present in Group I cartilaginous fishes, then such projections would be present in all jawed vertebrate groups with the exception of frogs. Such projections would thus be a generalized (plesiomorphic) feature of jawed vertebrates and would have been lost in the ancestral stock of frogs.

With a similarly sparse amount of data, we can tentatively argue that tectal input relayed from the striatum may be an apomorphy (specialization) of tetrapods, present in frogs (if not salamanders) and in amniotes. Such connections might be related to motor behaviors related to quadrupedal locomotion on land.

Ascending tectal projections to the dorsal thalamus are better understood, although more information is needed here as well. Tectal projections to at least two separate thalamic nuclei are present in all vertebrate groups studied to date: Group II cartilaginous fishes and the ray-finned fishes and tetrapods in both Groups I and II. This distribution suggests that such projections were present in the ancestral group of jawed vertebrates. It is probable, in fact, that they were present even earlier in the first definitive vertebrates. The optic tectum has a minor projection to one dorsal thalamic nucleus that also receives a substantial and direct retinal input, variously called nucleus anterior, the dorsal lateral geniculate nucleus, or other terms. In addition, the optic tectum has a major projection to one or more dorsal thalamic nuclei that do not receive direct retinal input. In nonmammalian vertebrates, only one such nucleus has been identified. It is called the dorsal posterior nucleus in anamniotes and nucleus rotundus in reptiles and birds. In mammals, two sets of tectal-recipient nuclei are present—the lateral posterior/pulvinar complex and the posterior nuclear group. The evolutionary relationship of these two tectofugal systems in mammals to the tectorotundal/dorsal posterior system of nonmammalian vertebrates is currently the subject of much debate.

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Part Four

THE FOREBRAIN: DIENCEPHALON

19

Overview of the Forebrain

INTRODUCTION

The forebrain consists of two parts—the **diencephalon** and the **telencephalon** (Fig. 19-1), which are extensively interconnected. This chapter is partly an overview of the forebrain, as the title proclaims, but it is more extensive than the previous overview chapters. Some parts of the forebrain, particularly the telencephalic pallium, some of the nuclei in the ventral thalamus, and the striatum, need to be introduced in greater detail here than a simple overview would encompass in order to adequately deal with the content of some of the following chapters.

Four major divisions of the diencephalon are present in all vertebrates: the **epithalamus**, **dorsal thalamus**, **ventral thalamus**, and **hypothalamus**. These divisions were recognized by Charles Judson Herrick early in this century from his studies of vertebrate embryos. Caudal to the thalamus, in a transition zone between the diencephalon and the mesencephalon, are two additional regions: the **pretectum** dorsally and the **posterior tuberculum** ventrally.

Most structures within the telencephalon can be assigned either to its dorsal part, the **pallium**, or its ventral part, the **subpallium** (Fig. 19-1). In vertebrates with everted telencephalons, i.e., ray-finned fishes, recent evidence indicates that at least some comparable divisions of the pallium of other vertebrates are present in the dorsal part of the telencephalon, at least in the majority of taxa in this large and diverse group. In vertebrates with evaginated telencephalons, the pallium is divided into several major regions. A **medial** (hippocampal) **pallium** and a **lateral pallium** are consistently present.

Between the medial and lateral pallia is the **dorsal pallium**, and ventral to the lateral pallium is a recently recognized fourth pallial component, the **ventral pallium**.

While consensus has been achieved on medial pallial identity and evolution across tetrapods, the derivatives of the dorsal, lateral, and ventral pallia and their homologous relationships are a focus of current research on several fronts, including their connectivity, gene expression patterns, and embryological development. In mammals, the expansive region of **neocortex** lies between the medial and lateral cortices. Deep to the lateral-most part of neocortex is a large group of diverse nuclei, collectively called the **amygdala**, most of which are part of the pallium. An additional pallial component in mammals is called the **claustrum-endopiriform formation**, which consists of a deeply situated layer of gray matter immediately dorsal to the amygdala. In contrast to mammals, sauropsids have two major pallial areas that are in receipt of ascending sensory projections—1) an area of cortex that comprises the **dorsal** (general) **cortex** and **pallial thickening** in reptiles, which is a larger, more elaborate area in birds called the **Wulst**, and 2) a large noncortical region called the **dorsal ventricular ridge (DVR)**. The relationship of the sauropsid DVR to components of the mammalian neocortex, pallial amygdala, and/or claustrum-endopiriform formation is a matter of continuing debate.

The ventral part of the telencephalon contains two major areas in all vertebrates, the **striatopallidal complexes** and the **septum**, as well as additional nuclei and cell populations that lie ventral to them. Among the latter are two nuclei of the amygdala that are subpallial and in fact components of the striatum.

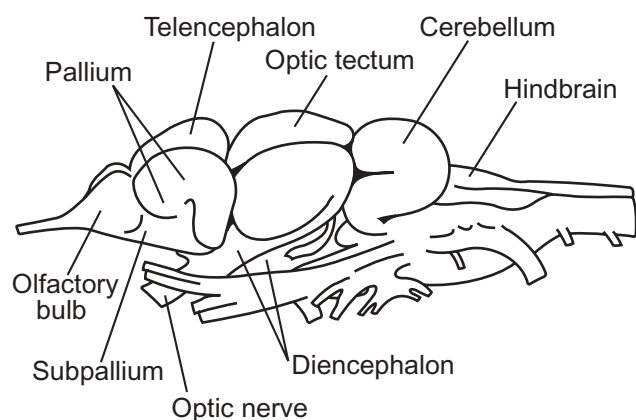


FIGURE 19-1. Lateral view of the brain of a longnose gar. Adapted from Northcutt and Butler (1976).

NOMENCLATURE OF THE FOREBRAIN IN AMNIOTES

A great deal of research has been done on the sensory systems of vertebrates, but the majority of studies have concentrated on a remarkably small number of species. In the diencephalon, as in other parts of the brain, nuclei are named according to a variety of principles. Most names are based on anatomical location (nucleus dorsomedialis, nucleus rostro-lateralis). Some others are named according to their shape (nucleus rotundus, nucleus ovoidalis, nucleus sphericus). Still others are named according to more fancifully descriptive associations evoked in the minds of the early anatomists who first described them (pulvinar, which means pillow; geniculate, which means knee-like). A complicating factor has been the use of different names for some of the neural structures, in both the telencephalon and diencephalon in different species and by different investigators studying the same species. A second and highly important issue that affects nomenclature is the still unresolved set of questions of homology between various forebrain components, particularly in the pallium, across amniotes.

In this text, we will use as the mammalian nomenclature the names that seem to be the most common, which are the ones used most often (but not always) for rodents, cats, and/or a number of primate species. Likewise, for reptiles we will use the most commonly used terms, although when several terms are in wide usage, we will provide the most common variants.

For the avian telencephalon, a revised nomenclature recently has been introduced. As noted in Chapter 15, this new set of terms was developed through extensive discussions among a number of avian and other comparative neurobiologists, and it was further honed and approved at The Avian Brain Nomenclature Forum, which was held at Duke University in July, 2002. This revised nomenclature employs the same terms as used in mammals in cases where homology is clear and compelling, such as for many of subpallial components, and neutral terms for structures that still remain to be fully understood, such as for a number of the components of the pallium. The latter terms replace previous terms with incorrect implications as to homology.

The revised avian nomenclature for telencephalic structures is summarized here in Tables 19-1 to 19-6. It should be noted that, not all of the structures listed in these tables are discussed in this textbook. Nonetheless, all of the new terms introduced as a result of the Forum are included here for the sake of completeness. It also should be noted that, for many of the new terms for pallial structures, the previously used abbreviations have been retained in order to facilitate a transition to the new terms and to bridge to the terminology in previously published literature. A direct comparison of the old and revised nomenclatures can be seen in the atlas of the brain of the collared dove (*Streptopelia decaocto*), recently published (2004) by Ardie den Boer-Visser, Martin Brittijn, and Jaap Dubbeldam.

THE DIENCEPHALON

During development, the periventricular matrix gives rise to neurons that either remain in situ or that migrate and form the nuclei of the various parts of the diencephalon. The degree of migration varies among Group I and Group II vertebrates. It also varies among the different parts of the diencephalon. Thus, different parts of the diencephalon are developed to a greater or lesser degree, depending on the particular group of vertebrates. In this section, we will survey the major sets of nuclei in each region of the diencephalon that are present when that region is relatively well developed.

Pretectum

The pretectum (Figs. 19-2 and 19-3) is a region that lies between the dorsal thalamus and the optic tectum. Its nuclei occupy **superficial, central, and periventricular** (or deep) **zones** (Fig. 19-2) that are in continuity with the superficial, central, and periventricular zones, respectively, of the optic tectum. A major commissural fiber tract, the **posterior commissure**, crosses the midline through the pretectal region, and a rostrocaudally running fiber tract, the fasciculus retroflexus (Fig. 19-3), courses through the periventricular part of the pretectal region. The major inputs to the pretectum are from the retina and the optic tectum. The efferent pathways of the pretectum are involved in the regulation of eye and body movements in relation to prey and other features of the visual world. The pretectum acts in concert with another nucleus or pair of nuclei that lie in the tegmentum and constitute the **accessory optic system**. The relations between the pretectum and the accessory optic system are discussed in Chapter 20.

Posterior Tuberculum

Ventral to the area of the pretectum is another transitional zone between the diencephalon and mesencephalon called the posterior tuberculum (Fig. 19-3). Migrated nuclei of the posterior tuberculum are present only in fishes. The unmigrated part of the posterior tuberculum was discussed in Chapter 17, as its cells contain dopamine and may be homologous as a field to the substantia nigra and ventral tegmental area of cartilaginous fishes and/or amniote vertebrates. Migrated nuclei of the posterior tuberculum, particularly those of the perglomerular nuclear complex (Figs. 19-3 and 19-4), relay sensory informa-

TABLE 19-1. Revised Terminology for Avian Subpallium

Karten-Hodos (1967) or Other Previous Term	Karten-Hodos (1967) or Other Previous Abbreviation	Revised Latin Term	Revised Latin Abbreviation	Revised English Term	Revised English Abbreviation
Lobus parolfactorius (excluding its rostral ventromedial part)	LPO (excluding its rostral ventromedial part)	Striatum mediale	StM	Medial striatum	MSt
Area X within male songbird LPO	X	Area X	X	Area X	X
Vocal control region in parrot LPO termed magnocellular nucleus of LPO	LPOm	Striatum mediale, pars magnocellularis	StMm	Magnocellular part of medial striatum	MStm
Paleostriatum augmentatum	PA	Striatum laterale	StL	Lateral striatum	LSt
Paleostriatum primitivum	PP	Globus pallidus	GP	Globus pallidus	GP
Nucleus intrapeduncularis	INP	Nucleus intrapeduncularis	INP	Intrapeduncular nucleus	INP
Ventromedial part of rostral lobus parolfactorius	—	Nucleus accumbens	Ac	Nucleus accumbens	Ac
Tuberculum olfactorium	TO	Tuberculum olfactorium	TuO	Olfactory tubercle	OTu
Unnamed circumscribed region between LPO and quinfofrontal tract (also referred to as ventral paleostriatum)	(VP or PVt)	Pallidum ventrale	PVt	Ventral pallidum	VP
Nucleus accumbens	Ac	Nucleus striae terminalis lateralis	NSTL	Lateral part of the bed nucleus of the stria terminalis	BSTL
Unnamed region around the lateral edge of the anterior commissure	—	Nucleus striae terminalis medialis	NSTM	Medial part of the bed nucleus of the stria terminalis	BSTM
Previously undefined cholinergic cell group within the medial forebrain bundle	—	Nucleus basalis magnocellularis	NBM	Basal magnocellular cholinergic nucleus	NBM
Region of fasciculus of diagonal band	FDB	Nucleus diagonalis Brocae	NDB	Nucleus of the diagonal band	NDB
Nucleus septalis medialis	SM	Nucleus septalis medialis	SM	Medial septal nucleus	SM
Nucleus septalis lateralis	SL	Nucleus septalis lateralis	SL	Lateral septal nucleus	SL

tion to the telencephalon from the lateral line and gustatory systems. These pathways through the migrated nuclei of the posterior tuberculum are similar to sensory pathways through dorsal thalamic nuclei in their organization. The migrated tubercular nuclei are not homologous, however, to any known nuclei in tetrapod vertebrates.

Epithalamus

The epithalamus is the most dorsal part of the diencephalon. In most vertebrates, it is composed of two major parts: the **pineal gland** and the **habenula** (Figs. 19-4 and 19-5). In some vertebrates, the epithalamus also includes a **pari-**

TABLE 19-2. Revised Terminology for Avian Wulst, Now Also Known as Hyperpallium

Karten-Hodos (1967) or Other Previous Term	Karten-Hodos (1967) or Other Previous Abbreviation	Revised Latin Term	Revised Latin Abbreviation	Revised English Term	Revised English Abbreviation
Hyperstriatum accessorium	HA	Hyperpallium apicale	HA	Apical part of hyperpallium	HA
Nucleus intercalatus hyperstriatum accessorium	IHA	Nucleus interstitialis hyperpallii apicalis	IHA	Interstitial part of the hyperpallium apicale	IHA
Hyperstriatum intercalatus superior	HIS	Hyperpallium intercalatum	HI	Intercalated part of the hyperpallium	HI
Hyperstriatum dorsale	HD	Hyperpallium densocellulare	HD	Densocellular part of hyperpallium	HD

TABLE 19-3. Revised Terminology for Avian Hyperstriatum Ventrale, Now Known As Mesopallium

Karten-Hodos (1967) or Other Previous Term	Karten-Hodos (1967) or Other Previous Abbreviation	Revised Latin Term	Revised Latin Abbreviation	Revised English Term	Revised English Abbreviation
Hyperstriatum ventrale	HV	Mesopallium	M	Mesopallium	M
Hyperstriatum ventrale dorsoventrale	HVdv	Mesopallium dorsale	MD	Dorsal mesopallium	MD
Hyperstriatum ventrale ventroventrale	HVvv	Mesopallium ventrale	MV	Ventral mesopallium	MV
Oval nucleus of the hyperstriatum ventrale in parrots	HVo	Nucleus ovalis mesopallii	MO	Oval nucleus of the mesopallium	MO
Caudal medial hyperstriatum ventrale	CMHV	Mesopallium caudomediale	CMM	Caudomedial mesopallium	CMM
Intermediate medial hyperstriatum ventrale	IMHV	Mesopallium intermediomediale	IMM	Intermediate medial mesopallium	IMM

etal eye. The epithalamus is involved with the maintenance of circadian rhythms in response to the light cycle and is part of a major pathway for the integration of limbic and striatal systems. The major afferent fiber tract to the habenula is the **stria medullaris** (Fig. 19-5), and its major efferent fiber tract is the **fasciculus retroflexus** (Fig. 19-3), by which it projects to the interpeduncular nucleus in the midbrain tegmentum.

Dorsal Thalamus

The dorsal thalamus (Figs. 19-4 and 19-5) is the main gateway to the telencephalon. It includes nuclei that relay sensory information to the telencephalon and, in some vertebrates, nuclei that are primarily involved in circuits with pallial areas of the telencephalon. The greater part of the sensory

information that reaches dorsal thalamic nuclei originates on the opposite, or contralateral, side of the body or space. In anamniotes, a significant portion of the dorsal thalamic projections to the telencephalon are bilateral, while the rest are restricted to the telencephalon on the same, or ipsilateral, side. In amniotes, dorsal thalamic projections to the ipsilateral telencephalon predominate, but some bilateral pathways are present.

The **medial** and **lateral forebrain bundles** are a set of fiber tracts that course through the diencephalon, connecting telencephalic and diencephalic regions with each other and with more caudal parts of the brain. Another major fiber tract of the diencephalon is the **optic tract**, which is the continuation of the optic nerve past the **optic chiasm**; most or all of the retinal ganglion cell axons in the optic nerve cross to the contralateral side of the brain via the optic chiasm. The axons

TABLE 19-4. Revised Terminology for Avian Neostriatum, Now Known As Nidopallium, and Its Subdivisions

Karten-Hodos (1967) or Other Previous Term	Karten-Hodos (1967) or Other Previous Abbreviation	Revised Latin Term	Revised Latin Abbreviation	Revised English Term	Revised English Abbreviation
Neostriatum	N	Nidopallium	N	Nidopallium	N
Neostriatum frontale	NF	Nidopallium frontale	NF	Frontal nidopallium	NF
Neostriatum intermedium	NI	Nidopallium intermedium	NI	Intermediate nidopallium	NI
Neostriatum caudale	NC	Nidopallium caudale	NC	Caudal nidopallium	NC
Neostriatum caudolaterale	NCL	Nidopallium caudolaterale	NCL	Caudolateral nidopallium	NCL
Ectostriatum	E	Entopallium or nucleus entopallialis	E	Entopallium or the entopallial nucleus	E
Nucleus basalis	Bas	Nucleus basorostralis pallii	Bas	The basorostral pallial nucleus	Bas
Field L	L	Area L pallii	L	Field L	L
Nidopallial area mistakenly called caudal nucleus of the hyperstriatum ventrale	HVc	HVC	—	HVC	—
Lateral magnocellular nucleus of the anterior neostriatum	LMAN	Nucleus lateralis magnocellularis nidopallii anterioris	LMAN	Lateral magnocellular nucleus of anterior nidopallium	LMAN
Medial magnocellular nucleus of the anterior neostriatum	mMAN	Nucleus medialis magnocellularis nidopallii anterioris	MMAN	Medial magnocellular nucleus of anterior nidopallium	MMAN
Nucleus interface of the neostriatum	NIf	Nucleus interfaccialis nidopallii	NIf	Nucleus interface of the nidopallium	NIf
Caudomedial neostriatum	NCM	Nidopallium caudomediale	NCM	Caudal medial nidopallium	NCM
Oval nucleus of the anterior neostriatum in parrots	NAo	Nucleus ovalis nidopallii anterioris	NAO	Oval nucleus of the anterior nidopallium	NAO
Medial oval nucleus of the anterior neostriatum in parrots	NAom	Nucleus ovalis nidopallii anterioris, pars medialis	NAOM	Medial part of the oval nucleus of the anterior nidopallium	
Central nucleus of the lateral neostriatum in parrots	NLc	Nucleus centralis nidopallii lateralis	NLC	Central nucleus of the lateral nidopallium	NLC

in the optic tract project to sites in the diencephalon and to the optic tectum.

In Chapter 22, we will introduce the various nuclei and nuclear groups of the dorsal thalamus. In most anamniote vertebrates, only three dorsal thalamic nuclei are present; in contrast, amniotes have a greatly expanded dorsal thalamus consisting of many nuclei and/or nuclear groups. The organizational plan of the dorsal thalamus in each of the major radiations of vertebrates, including mammals, is similar. The mammalian dorsal thalamus does have a number of derived (apomorphic) features, which, when identified and separated out, reveal the presence of the same basic features of the dorsal thalamus common to all vertebrates. Dorsal thalamic nuclei can be divided into two categories in all vertebrates:

- A **lemnothalamus** comprises nuclei that are predominantly in receipt of lemniscal (i.e., direct projections not involving a midbrain roof relay) retinal, somatosensory, and other afferents.
- A **collothalamus** comprises nuclei that are predominantly in receipt of sensory inputs relayed to them from the roof of the midbrain.

Ventral Thalamus

The ventral thalamus lies ventral to the dorsal thalamus and is involved with some sensory processing and with motor control systems. We will discuss some of these nuclei in detail in this chapter, since a separate chapter will not be devoted to

TABLE 19-5. Revised Terminology for Avian Archistriatum, Now Known As Arcopallium, and Its Subdivisions

Karten-Hodos (1967), or Other Previous Term	Karten-Hodos (1967) or Other Previous Abbreviation	Revised Latin Term	Revised Latin Abbreviation	Revised English Term	Revised English Abbreviation
Archistriatum and Subdivisions, Now Known As Arcopallium and Subdivisions					
Archistriatum	A	Arcopallium	A	Arcopallium	A
Nucleus archistriatalis anterior	AA	Arcopallium anterius	AA	Anterior arcopallium	AA
Archistriatum, pars dorsalis, or archistriatum intermedium, pars dorsalis	Ad, or Aid	Arcopallium dorsale	AD	Dorsal arcopallium	AD
Upper part of archistriatum, pars ventralis, or archistriatum intermedium	Upper part of Av, or Ai	Arcopallium intermedium	AI	Intermediate arcopallium	AI
Medial part of archistriatum, pars ventralis, or archistriatum mediale	Am	Arcopallium mediale	AM	Medial arcopallium	AM
Robust nucleus of archistriatum in songbirds	RA	Nucleus robustus arcopallii	RA	Robust nucleus of arcopallium	RA
Central nucleus of anterior archistriatum in parrots	AAC	Nucleus centralis arcopallii anterioris	AAC	Central nucleus of anterior arcopallium	AAC
Archistriatum Subdivisions, Now Known As Amygdalar Subdivisions					
Ventral part of archistriatum, pars ventralis plus caudal part of archistriatum, or archistriatum posterior	Ap	Nucleus posterioris amygdalopallii	PoA	Posterior pallial amygdala	PoA
Nucleus taeniae	Tn	Nucleus taeniae amygdalae	TnA	Nucleus taeniae of the amygdala	TnA
Region below paleostriatum primitivum posterior to anterior commissure	Ventral part of PA	Area subpallialis amygdalae	SpA	Subpallial amygdaloid area	SpA

TABLE 19-6. Terminology Retained for Avian Hippocampal and Corticoid Areas

Karten-Hodos (1967), or Other Previous Term	Karten-Hodos (1967) or Other Previous Abbreviation	Retained Latin Term	Retained Latin Abbreviation	Retained English Term	Retained English Abbreviation
Area parahippocampalis	APH	Area parahippocampalis	APH	Parahippocampal area	APH
Hippocampus	Hp	Hippocampus	Hp	Hippocampus	Hp
Cortex piriformis	CPi	Cortex piriformis	CPi	Piriform cortex	CPi
Area corticoidea dorsolateralis	CDL	Area corticoidea dorsolateralis	CDL	Dorsolateral corticoid area	CDL
Area tempero-parieto-occipitalis	TPO	Area tempero-parieto-occipitalis	TPO	Tempero-parieto-occipital area	TPO

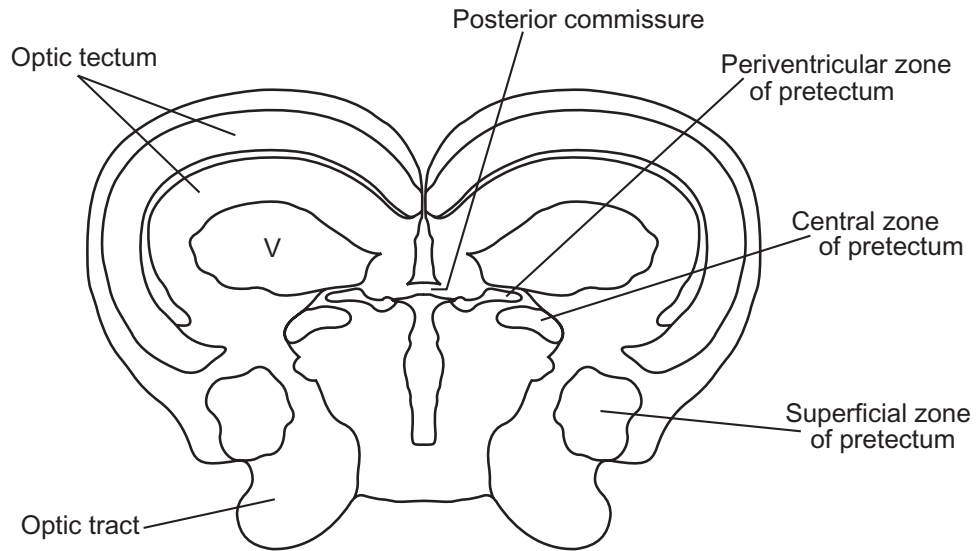


FIGURE 19-2. Drawing of a transverse section through the pretectum and posterior tuberculum of a herring (*Clupea harengus*). Adapted from Butler and Northcutt (1993). Note that in this figure and in figures in this and succeeding chapters on the forebrain, ventricular spaces are either not labeled or are indicated by the abbreviation V.

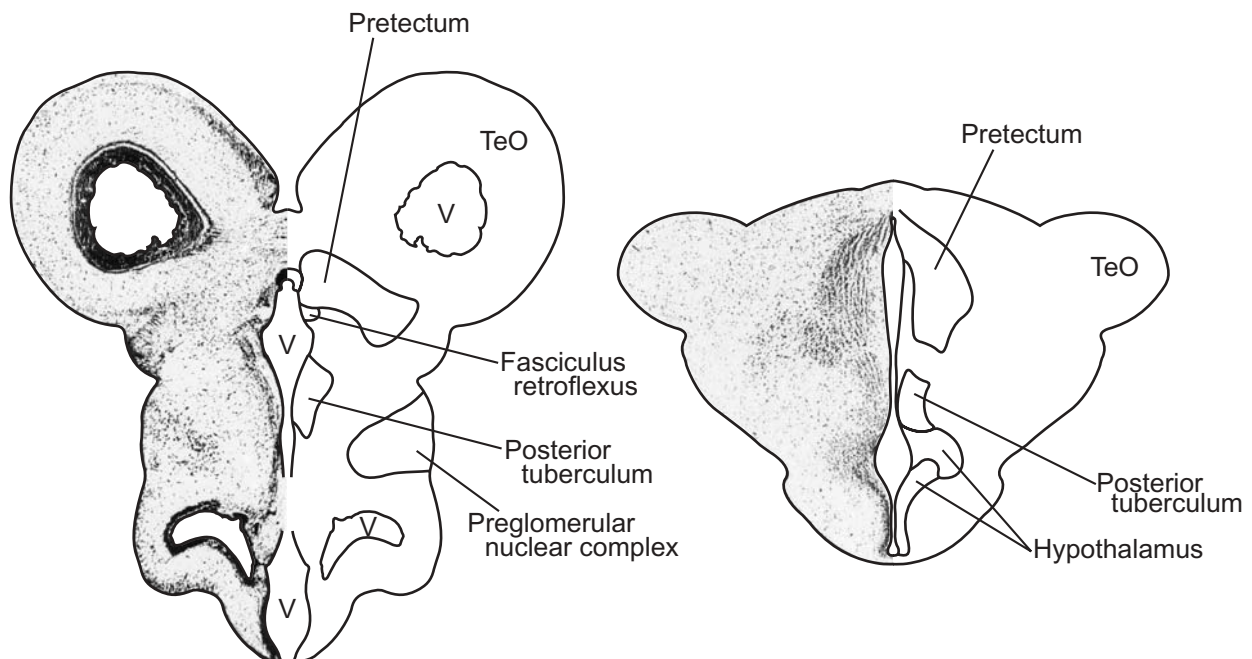


FIGURE 19-3. Transverse hemisections with mirror image drawings through the pretectum and posterior tuberculum of the bowfin (*Amia calva*) on the left and a bullfrog (*Rana catesbeiana*) on the right. Adapted from Butler and Northcutt (1992) and Wilczynski and Northcutt (1983), respectively. Material from the former used with permission of S. Karger AG, Basel and from the latter with permission of John Wiley & Sons.

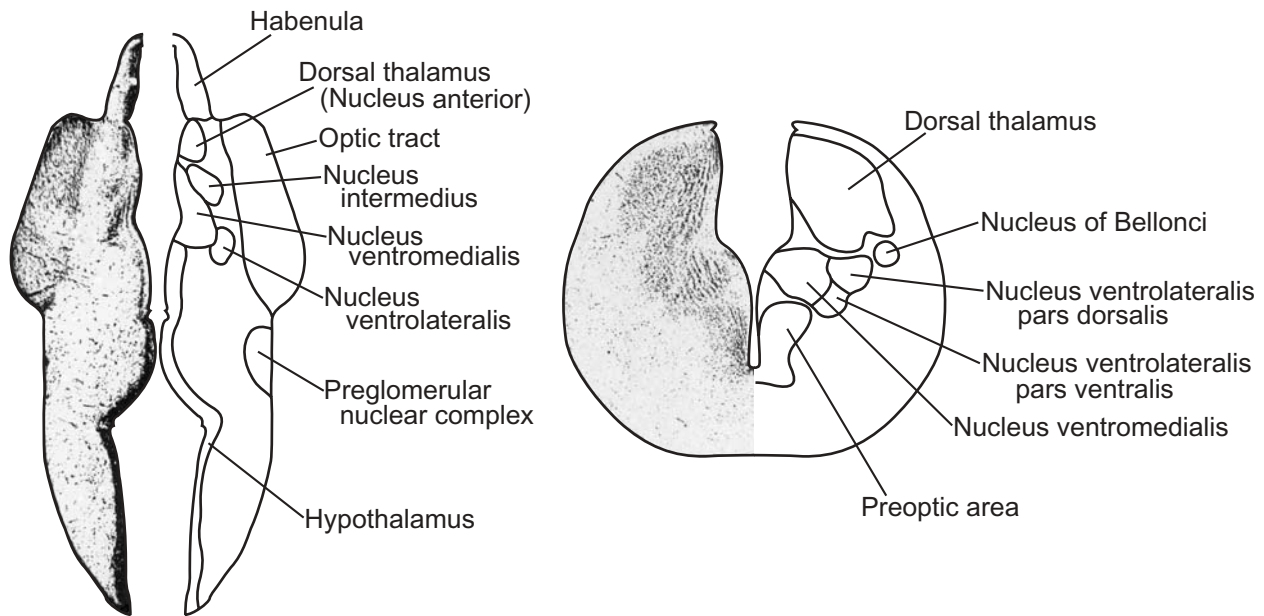


FIGURE 19-4. Transverse hemisections with mirror-image drawings through the diencephalon of the bowfin (*Amia calva*) on the left and the bullfrog (*Rana catesbeiana*) on the right. Adapted from Butler and Northcutt (1992) and Wilczynski and Northcutt (1983), respectively. Material from the former used with permission of S. Karger AG, Basel and from the latter with permission of John Wiley & Sons.

the ventral thalamus. The other major nuclei within the ventral thalamus are related to motor control and will be discussed in Chapter 24 on the basal telencephalon.

In most anamniotes, at least three nuclei are present in the ventral thalamus. In cartilaginous and ray-finned fishes, these nuclei (Fig. 19-4) have been termed **nucleus intermedius**, **nucleus ventromedialis**, and **nucleus ventrolateralis**. These nuclei all receive retinal projections, but most of their other connections remain to be investigated. In amphibians (Fig. 19-4), a nucleus ventromedialis and dorsal and ventral divisions of nucleus ventrolateralis have been recognized. Also present in a more lateral position is a nucleus that receives a heavy retinal projection and is called the **nucleus of Bellonci**. Its caudal continuation is a cell sparse area, the **neuropil of Bellonci**. This nucleus was long thought to be a dorsal thalamic visual relay to the telencephalon, but it has no telencephalic projections and is now assigned to the ventral thalamus. Whether it might correspond to the nucleus intermedius of ray-finned fishes is an open question.

Among amniotes, the ventral thalamus has been most extensively studied in mammals in which it is frequently referred to as the **subthalamus**. The ventral thalamus of mammals contains three nuclei that are interconnected primarily with the globus pallidus of the subpallium and the substantia nigra and that play a role in motor control (see Chapter 24). In nonmammalian amniotes, the ventral thalamus also contains four or more nuclei, two of which are **nucleus ventromedialis** and **nucleus ventrolateralis** (Fig. 19-5). The ventrolateral nucleus receives a minor input from the retina, but most other connections of these two nuclei remain to be investigated.

Lateral Geniculate Nucleus Pars Ventralis. In all amniotes, the ventral thalamus contains a nucleus called the **ventral part** (or the **pars ventralis**) of the **lateral geniculate nucleus**, also referred to as the **ventral lateral geniculate nucleus**. This nucleus receives projections from the retina, optic tectum, and other visual system components and is involved in visual functions, particularly in regard to eye movements. The ventral lateral geniculate nucleus does not project to the telencephalon as do the collothalamic and lemnothalamic visual nuclei of the dorsal thalamus. It participates instead in brainstem visual pathways. In reptiles and birds, the ventral lateral geniculate nucleus is of substantial size and forms an oval or lens-shaped nuclear mass that curves around the lateral edge of the diencephalon (Fig. 19-5). In reptiles, this nucleus consists of a lateral neuropil region that curves along the lateral edge of a more medially lying cell plate. Immediately dorsal to it is another, related component of the ventral thalamus, the **intergeniculate leaflet**. (This nucleus has been identified previously as two nuclei—*geniculatus lateralis pars dorsalis* and *intercalatus*, among other terms. In the first edition of this textbook, both of these nuclei were included within the area labeled as the dorsal lateral optic nucleus.) A third, visually related, ventral thalamic component lies rostral to the dorsal lateral geniculate nucleus (see Chapter 22) and is called **nucleus ovalis**. All of these ventral thalamic visual nuclei receive retinal projections; they are variously interconnected with hypothalamic, tectal and other brainstem sites.

In mammals, the position of the ventral lateral geniculate nucleus varies substantially, depending on the degree of development, expansion, and rotation of the dorsal lateral geniculate nucleus. Among primates, the ventral lateral geniculate nucleus is known as the **pregeniculate nucleus**, since it lies

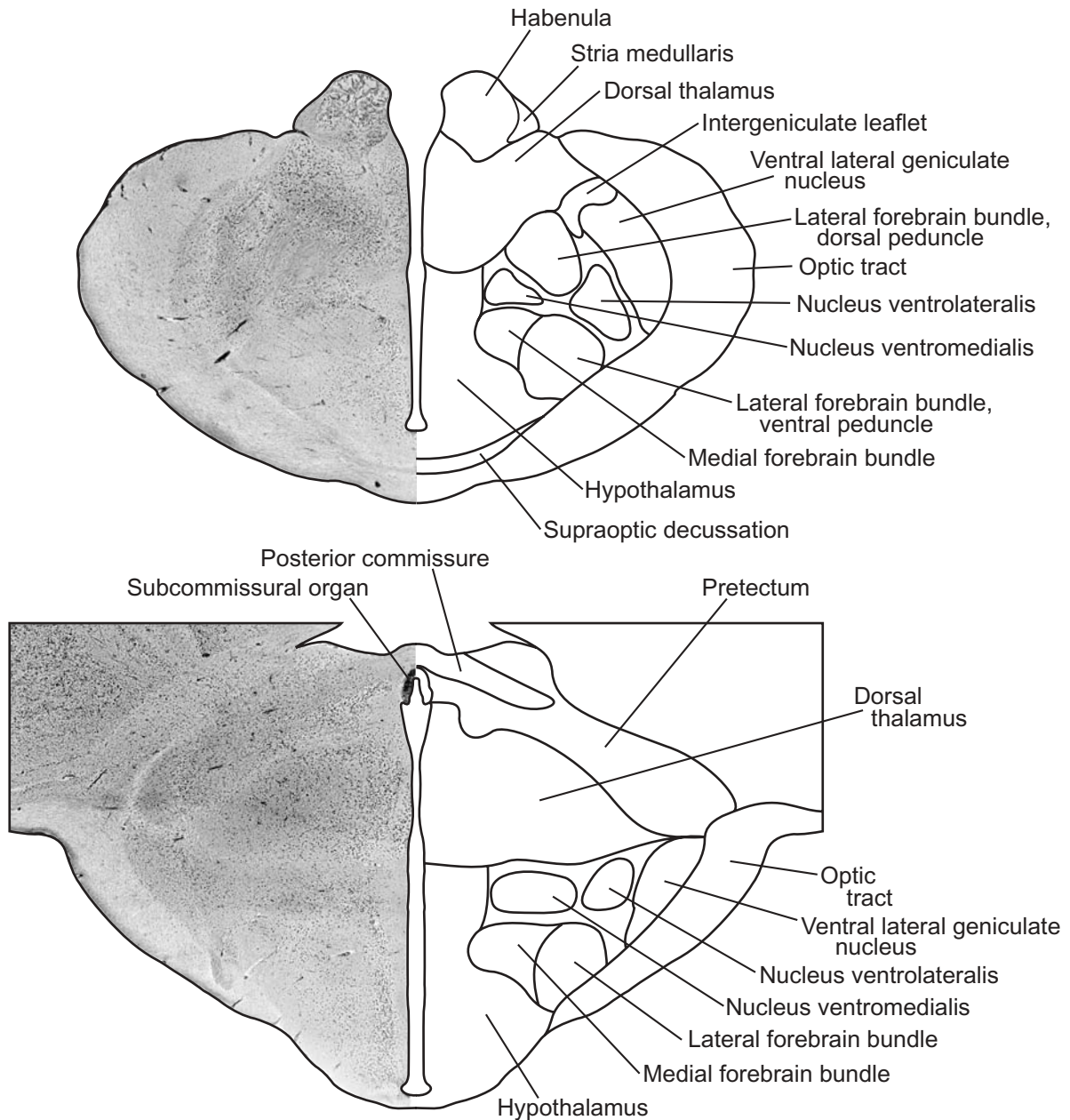


FIGURE 19-5. Transverse hemisections with mirror image drawings through the diencephalon of a lizard (*Iguana iguana*). The more rostral section is at the top. Adapted from Butler and Northcutt (1973) with ventral thalamic nuclei identifications based on Kenigfest et al. (1997).

dorsal to the dorsal lateral geniculate nucleus. In some mammals, particularly some rodents, the ventral lateral geniculate nucleus has two major divisions, a **dorsal zone** and a **ventral zone**. The latter is clearly laminated and is sometimes called the **external** or the **magnocellular division**. In the dorsal zone, the more ventral part is called the **internal** or the **parvocellular division**, and the dorsal part is called the **dorsal cap**. Like sauropsids, mammals also have an **intergeniculate leaflet**, which is a thin strip of cells that lies between the ventral and dorsal lateral geniculate nuclei.

The mammalian ventral lateral geniculate nucleus receives projections from the retina, several visual neocortical areas, pretectum, and the superficial (visual) and intermediate (multisensory and motor) zones of the superior colliculus. Its efferents, in turn, project back to the intermediate zone of the superior colliculus and to the pretectum. It also has connections with the cerebellum, via efferent projections to pontine nuclei. In turn, the cerebellum, which is reciprocally highly interconnected with the vestibular system, has a minor reciprocal output to the intermediate zone of the superior colliculus.

lus. As can be deduced from its connections, the ventral lateral geniculate nucleus plays a role in the regulation of eye movements in response to visual stimuli and in the coordination of eye and head movements.

In birds, several parts of the ventral lateral geniculate nucleus also have been identified. An intergeniculate leaflet is present, sometimes called the **nucleus of the marginal optic tract**, as is a dorsal cap region. The latter is usually identified in birds as the **nucleus lateralis anterior**. A **nucleus externus** comparable to the same division of the mammalian ventral lateral geniculate nucleus is also present. The connections of the ventral lateral geniculate nucleus in birds are similar to those in mammals, including its connections with the cerebellum and vestibular system via the pons. Its role in influencing eye movements appears to be conserved across amniotes.

Thalamic Reticular Nucleus. An additional ventral thalamic nucleus in mammals is the **thalamic reticular nucleus**, which is interconnected primarily with the nuclei of the dorsal thalamus and appears to be a rostral counterpart of the reticular formation of the hindbrain (see Chapter 13). The thalamic reticular nucleus is formed by a thin sheet of cells that enfolds the anterior, lateral, and ventral surfaces of the dorsal thalamus; the nucleus is traversed by axons that interconnect the telencephalon with the dorsal thalamus and the rest of the brainstem. The thalamic reticular nucleus receives projections from the neocortex and also a cholinergic input from nucleus cuneiformis in the isthmal region (see Chapter 16), a part of the reticular formation. All of the neurons of the thalamic reticular nucleus are GABAergic and also positive for parvalbumin, a calcium-binding protein that frequently occurs in association with GABAergic neurotransmission. These neurons provide short latency, recurrent inhibitory input to the dorsal thalamic relay nuclei bilaterally.

A thalamic reticular nucleus has also been identified in crocodiles and may thus be a common feature of amniotes. This nucleus, however, appears to be more complexly organized than its mammalian counterpart. The neuron cell bodies of the nucleus lie in a location similar to that of the thalamic reticular nucleus of mammals, scattered among axons of the dorsal part, or peduncle, of a major fiber tract, the lateral forebrain bundle (Fig. 19-5), that interconnects the telencephalon with the rest of the brain. The neurons of the thalamic reticular nucleus project to the nuclei of the dorsal thalamus, as is the case in mammals, but they are not GABAergic. A small number of GABAergic neurons are present in the region but do not project to the dorsal thalamus. Some of the thalamic reticular neurons are positive for parvalbumin, and others are not. Thus, several subpopulations of neurons are present in this nucleus in crocodiles, whereas only one population of neurons appears to constitute the homologous nucleus in mammals.

In birds, the thalamic reticular nucleus, called the **pars dorsalis of the superior reticular nucleus**, is also present. Less is known about its histochemistry than in crocodiles, but like the thalamic reticular nucleus of mammals, it does contain GABAergic neurons. Also as in mammals, this nucleus lies in a comparable position and projects to dorsal thalamic nuclei. Thus, the thalamic reticular nuclei of birds and mammals may represent one of many examples of parallel evolution in these

two radiations, most likely due to the expression of homologous genes and thus an additional example of syngeny.

Hypothalamus and Preoptic Area

The hypothalamus (Figs. 19-3–19-5) lies in the most ventral part of the diencephalon. The region rostral to the hypothalamus is called the **preoptic area**, named for its position immediately dorsal to the optic chiasm. The preoptic area forms the rostralmost part of the diencephalon and is functionally related to the hypothalamus. The hypothalamus and preoptic area are primarily involved with the regulation of the internal organ systems of the body. The nuclei in these regions are connected with the hypophysis (pituitary) by fiber connections and hormonal systems. The preoptic area and hypothalamus are also widely connected with other parts of the brainstem and with the limbic system of the forebrain. A multitude of functions—including diurnal rhythms, reproductive behaviors, temperature regulation, feeding, drinking, sleeping, and emotional responses—are all under the control of or influenced by various parts of these regions.

THE TELENCEPHALON: PALLIUM

The telencephalic pallium in all vertebrates has three major divisions, although the question of whether these recognized divisions are homologous, each to each, as derivatives of embryonic fields or in other specified ways, across all groups of vertebrates has not been resolved. A fourth pallial division has recently been recognized as well. In Group I vertebrates with evaginated, laminar telencephalons (such as lampreys and squalomorph sharks), three divisions have generally been recognized and are often referred to by geographical names: medial, dorsal, and lateral (Fig. 19-6). In vertebrates with simply everted telencephalons, such as some ray-finned fishes, the mediolateral position of these cortices appears to be reversed

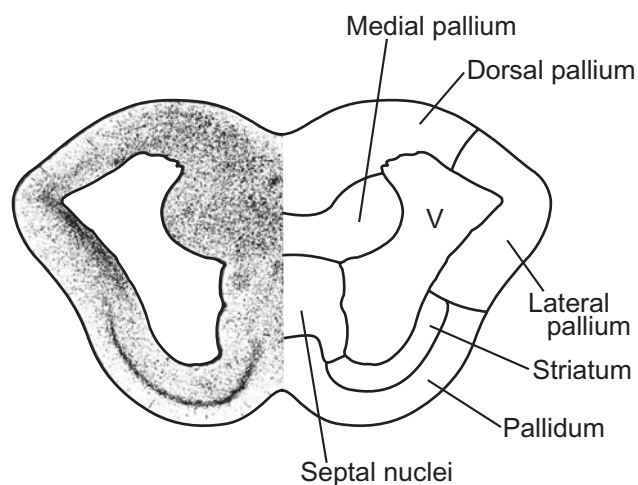


FIGURE 19-6. Transverse hemisection with mirror-image drawing through the telencephalon of a squalomorph shark (*Squalus acanthias*). Adapted from Northcutt et al. (1988) and used with permission of John Wiley & Sons.

(see Chapter 3), although whether all three of these regions are strict homologues of the medial, dorsal, and lateral pallia in vertebrates with evaginated telencephalons is a matter of debate. In the everted brain, the “medial” pallium is in a lateral, or distal, position, and the “lateral” pallium is in a medial, or proximal, position. In ray-finned fishes that have Type I brains with little cell migration away from the ventricular surface, i.e., bichirs, the pallial regions have been designated previously as P1, P2, and P3, with P1 in the most medial, or proximal, position. More recent findings suggest that P2 and P3 actually constitute one distal division called the **dorsolateral pallium**, while P1 comprises the proximal division, the **dorsomedial pallium** (Fig. 19-7).

In vertebrates with evaginated telencephalons, the medial pallium also can be referred to as the hippocampal pallium, a telencephalic part of the limbic system that is interconnected with the septum and the hypothalamus. The term hippocampal pallium can similarly be used to refer to the putatively homologous lateral, or distal, pallium in teleosts. Likewise, the adjectives **olfactory** or **piriform** can be used to refer to part of the lateral pallium in vertebrates with evaginated telencephalons. The olfactory pallium, or primary olfactory cortex, is in receipt of projections relayed to it from the olfactory bulb. The olfactory bulb also projects directly to parts of the amygdala.

In the Type I pallia of frogs (Fig. 19-8), four pallial divisions recently have been identified on the basis of gene expression patterns. The medial pallium is relatively expanded with some degree of cell migration and expansion, even in these Type I brains. It receives a substantial, bilateral, ascending, sensory input from the rostral part of the dorsal thalamus. The dorsal pallium is very limited, a small zone wedged between the medial and lateral pallia. The lateral pallium shows very little cell migration. Most of its neurons are tightly packed in the juxtaventricular layer. Much of the lateral pallium is in receipt of olfactory projections. The ventral pallium lies ventral to the lateral pallium and has two components. The first is a region

previously identified as the ventral division of the lateral pallium, now identified as the lateral part of the amygdala. It is in receipt of some ascending sensory inputs from the more caudal part of the diencephalon. Part of the region identified as the medial amygdala is also pallial and also a derivative of the ventral pallium. This part of the amygdala is in receipt of olfactory projections.

In hagfishes (Fig. 19-9), the telencephalon is markedly expanded. The telencephalon undergoes evagination during development; the pallial areas are enlarged and laminated, and all receive direct olfactory projections. The pallial areas have been designated as **P1–P5**, with P1 being the most superficial; no correspondence with the pallial areas P1–P3 in ray-finned fishes is meant to be implied by this terminology. The connections of the pallium in hagfishes need further study before comparisons can be made with other vertebrates.

Among Type II anamniotes with jaws, hippocampal (medial), dorsal, and olfactory (lateral) pallial divisions are present in sharks, skates and rays. The dorsal pallium includes a large region called the central nucleus (Fig. 19-10), which at some levels extends all the way to the midline. In teleosts with Type II brains, the migration of neurons away from the everted, periventricular surface during development makes it challenging to decipher the topographic relationships of regions within both the pallial and the striatal areas.

The Telencephalic Pallium of Mammals

In mammals (Fig. 19-11), the medial, hippocampal and lateral, olfactory cortices each have three cell and fiber layers. Most of the largest pallial component, the dorsal pallium, forms a six-layered cortex called **neocortex**, or **isocortex** (see Box 3-1) (Figs. 19-11 and 19-12). Cortex that lies in the transition zone between the three-layered cortices and neocortex and has an intermediate number of layers (4–5) is referred to as **transitional cortex**. The three-layered and transitional cortices are sometimes referred to as **allocortex**.

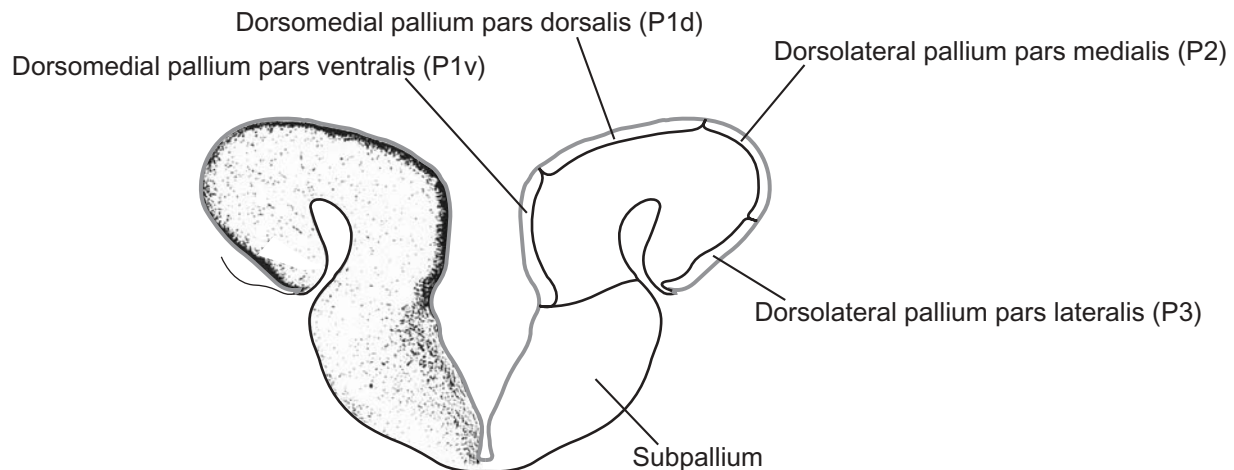


FIGURE 19-7. Transverse hemisection with mirror-image drawing through the telencephalon of a non-teleost ray-finned fish, the bichir (*Polypterus palmas*). Adapted from Reiner and Northcutt (1992) with pallial terminology from Holmes and Northcutt (2003) and used with permission of John Wiley & Sons.

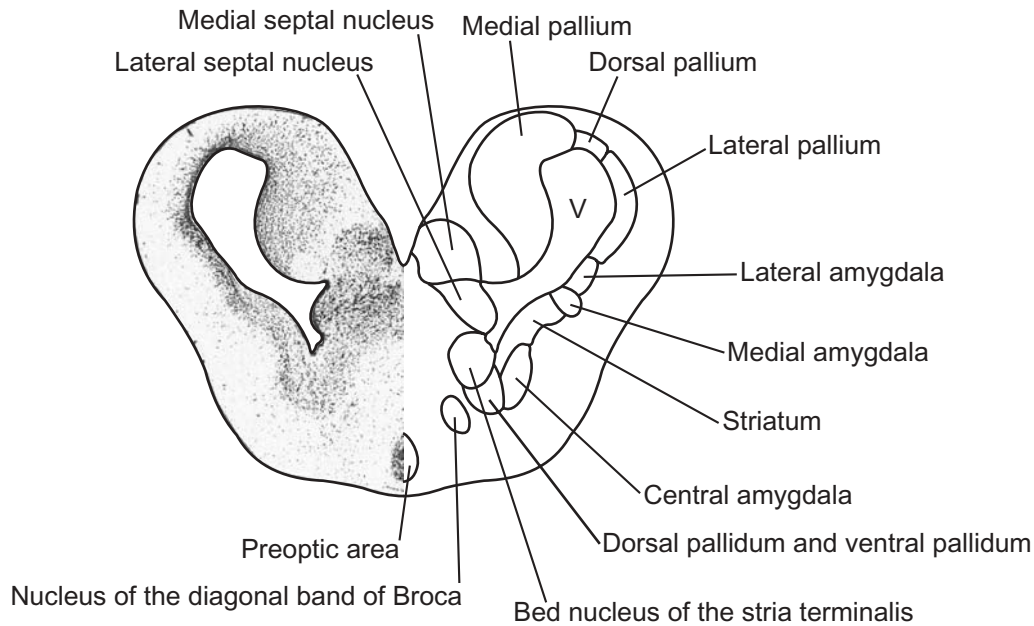


FIGURE 19-8. Transverse hemisection with mirror-image drawing through the telencephalon of a bullfrog (*Rana catesbeiana*). Nissl hemisection adapted from Wilczynski and Northcutt (1983) with subpallial nuclear boundaries and labels adapted from Marín et al. (1998) and used with permission of John Wiley & Sons.

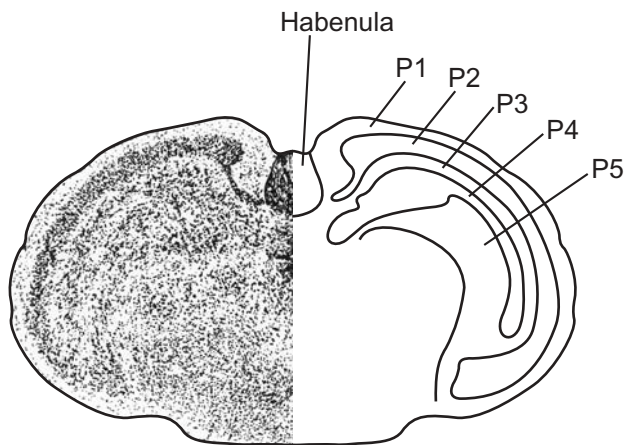


FIGURE 19-9. Transverse hemisection with mirror-image drawing through the telencephalon of a hagfish (*Eptatretus stouti*). Adapted from Wicht and Northcutt (1992) and used with permission of S Karger AG, Basel.

The outermost layer of neocortex, **layer I**, is the **molecular layer**. It is relatively cell sparse, consisting predominantly of afferent axons and the dendritic ramifications of neurons in deeper cortical layers. **Layer II** is called the **external granular layer**, in reference to its population of **granule cells**, relatively small neurons with short axons. **Layer III** is the **external pyramidal layer** and contains **pyramidal cells**, which have dendrites that extend from the apex of the cell soma toward the external surface of the cortex and are known as **apical dendrites**. Neurons in layers II and III give rise to projections to the deeper cortical layers, and their extrinsic

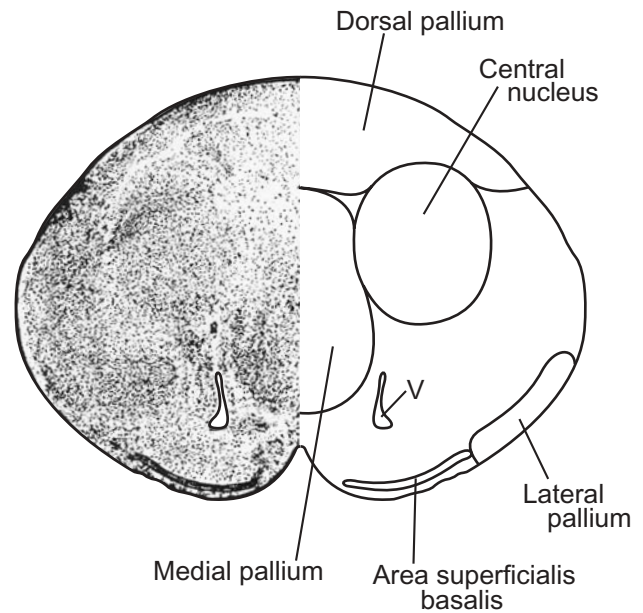


FIGURE 19-10. Transverse hemisection with mirror-image drawing through the telencephalon of a shark (*Ginglymostoma cirratum*). Adapted from Ebbesson (1980) and used with kind permission of Springer Science and Business Media.

projections are predominantly to other cortical areas, either contralaterally via the corpus callosum or to other ipsilateral cortical areas.

Layer IV is the **internal granular layer** and contains an abundance of granule cells. Layers II and VI are usually well developed in cortical areas that receive ascending sensory pro-

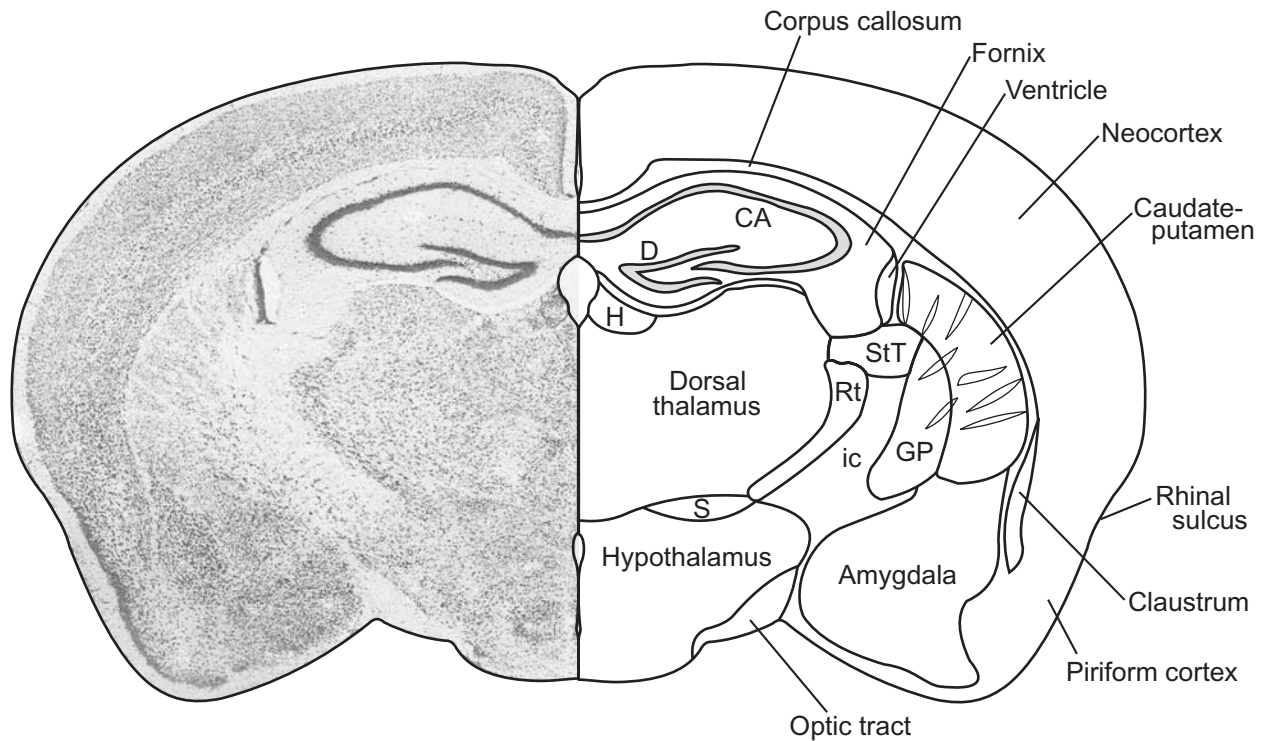


FIGURE 19-11. Drawing of a transverse hemisection through the right forebrain of a mouse (*Mus musculus*). Adapted from Slotnick and Leonard (1975). Abbreviations: CA, Ammon's horn; D, dentate gyrus; GP, globus pallidus; H, habenula; ic, internal capsule; Rt, thalamic reticular nucleus; S, subthalamus; StT, stria terminalis.

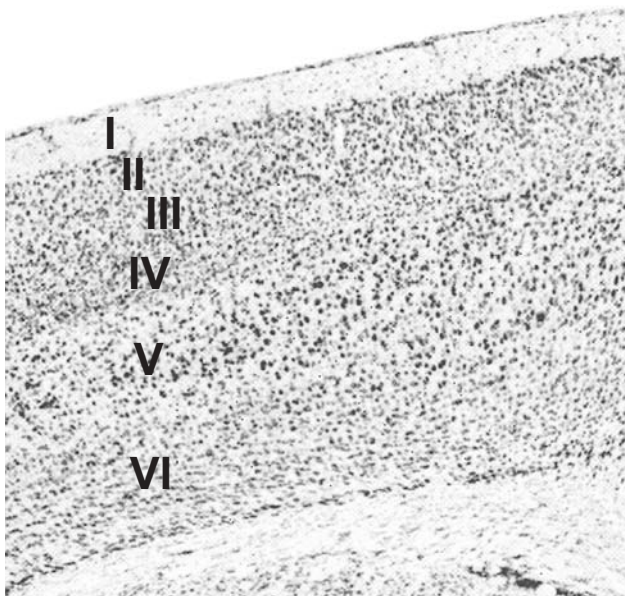


FIGURE 19-12. Medial part of neocortex in a mouse (*Mus musculus*), with the six layers indicated by Roman numerals. Adapted from Slotnick and Leonard (1975) with layering of the rodent cortex based on Zilles and Wree (1995).

jections from the dorsal thalamus, and this type of cortex therefore is called **granular cortex** or **koniocortex**. (The prefix "konio" is derived from the Greek word for dust, referring to the granulated appearance of the cortex.) Some mammals lack a well-developed layer IV, however, such as the hedgehog tenrec, a eulipotyphlan (the order previously known as insectivores), whose neocortex is illustrated in Figure 19-12. In contrast, a very prominent layer IV is shown in the visual cortex of a raccoon in Figure 26-6.

The **infragranular layers**, layers V and VI, give rise to the set of efferent cortical fibers that project to subcortical structures. Layer V is the **internal pyramidal layer**, and layer VI is called the **multiform layer**. Neurons in the latter are predominantly **fusiform cells**, which have elongated somata. Layer V neurons give rise to projections to the striatum, the superior colliculus, and the spinal cord, while layer VI neurons give rise to reciprocal projections to the dorsal thalamus. The pyramidal layers, layers III and V, rather than layers II and IV, are particularly well developed in cortical areas involved in motor control, and this type of cortex is therefore referred to as **agranular cortex**.

The neocortex has a columnar organization in that it is functionally organized as vertical **columns**, each about 300 μm in diameter, which extend perpendicularly through all six cortical layers. In sensory cortices, each column receives the input from a given peripheral receptive field, and the columns are arranged so that the topographic organization of the receptive fields is maintained.

In some mammals, the surface of the telencephalic hemispheres is relatively smooth (Fig. 19-13). This condition tends to characterize the brains of species within an order that have the smaller absolute brain and body sizes, and it is referred to as **lissencephalic**. In other mammals (Fig. 19-14), particularly those species within each order that have larger absolute brain and body sizes, the cerebral cortex is hypertrophied and is folded into **gyri** (singular = gyrus), or ridges, with **sulci** (singular = sulcus), or grooves, between them. This condition is referred to as **gyrencephalic**. During development in a gyrencephalic species, the crowns of the gyri grow outward, while the sulcal fundi remain relatively static (Fig. 19-15). Sometimes

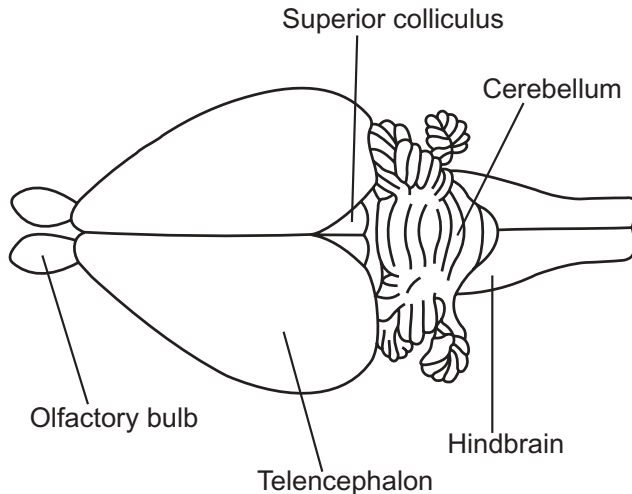


FIGURE 19-13. Dorsal view of a brain of a rabbit (*Lepus sp.*). Adapted from Northcutt (1979) and used with permission of The University of Chicago Press.

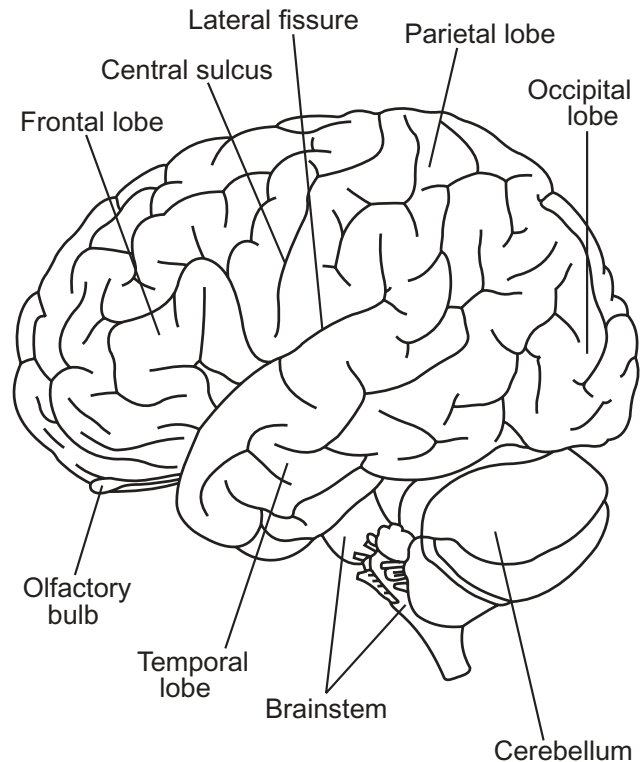


FIGURE 19-14. Lateral view of the brain of a primate (*Homo sapiens*). Adapted from Nieuwenhuys et al. (1978) and used with kind permission of Springer Science and Business Media.

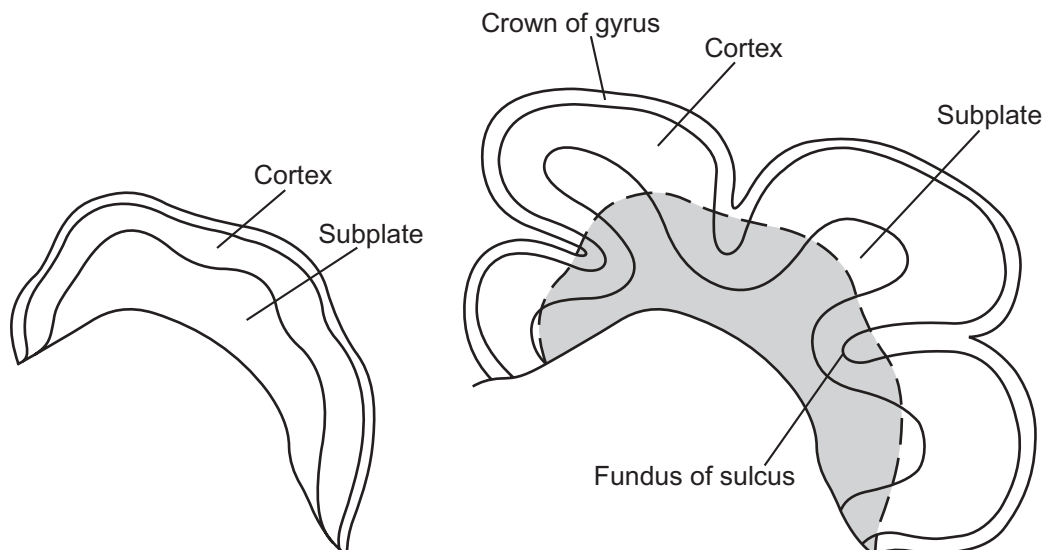


FIGURE 19-15. Development of gyri and sulci. Earlier stage in cortical development (left) shows the relative size and position of the developing subplate and cortex. Later stage (right) shows the subplate and cortex with gyral development and, indicated by shading, the earlier stage superimposed for comparison. Note that the sulcal fundi are near the surface of the earlier stage, while the gyral crowns have grown outward. Adapted from Welker (1990) and used with kind permission of Springer Science and Business Media.

the term **fissure** is used to denote particularly deep sulci, such as the grooves that separate the various lobes of the cerebral and cerebellar hemispheres. For certain other grooves, the terms sulcus and fissure are used interchangeably, as we do here.

Neocortex occupies the bulk of the cerebral hemispheres, which can be divided into **frontal**, **parietal**, **temporal**, and **occipital lobes** (Fig. 19-14). In gyrencephalic brains, two of the major grooves are the **central sulcus** (of Rolando), which divides the frontal from the parietal lobe, and the **lateral fissure**, or Sylvian fissure, which divides the temporal from the frontal and parietal lobes. An area of neocortex called **insular cortex** lies along the deep banks of the lateral sulcus. An additional sulcus to note here, the **rhinal sulcus**, or fissure, separates neocortex from olfactory cortex (Fig. 19-11).

The motor cortex and the somatosensory cortex are located in adjacent or, in some mammals, overlapping parts of the frontal and parietal lobes, respectively. The frontal lobes also contain a related premotor cortical area and the frontal eye fields, which are involved in the control of eye movements. In humans, a part of the frontal lobe called Broca's area is involved in the motor control of speech. Auditory cortex lies in the temporal lobe, and visual cortex is located in the occipital lobe. The so-called primary, or striate, visual cortex occupies the banks of the **calcarine fissure**, which is shown in Figure 19-16. Association cortices are present in addition to primary

sensory cortices. A large part of the frontal lobe called the **pre-frontal cortex** is regarded as an association cortex, although it also receives a substantial ascending sensory input from the dorsal thalamus. Association cortical areas are also present in the temporal and parietal lobes, lying between the auditory, somatosensory, and visual sensory cortical areas.

The delineation of the various neocortical areas and of their boundaries is an actively continuing topic of research. Boundaries are most often defined by changes in the cytoarchitecture (the pattern of cellular distribution) in the cortical layers and/or changes in maps of sensory representations as revealed by electrophysiology. Korbinian Brodmann, a German neurologist, was a pioneer of cytoarchitectonic studies. In 1908, Brodmann published a map of the human cortex, assigning a number to each of almost 50 identified regions. Many of these numbers are in the neuroscientific vernacular today, such as 3,1,2 for somatosensory cortex and 17 for the striate visual cortex.

A substantial range of variation exists between species in the pattern of gyri and sulci, where present, and in the extent and position of sensory and motor areas. These areas need to be identified in each species by studies tracing afferent connections or recording electrophysiological responses to stimulation. Sensory and motor areas identified in the brain of an echidna are shown in Figure 19-17. Variation in the pattern of gyri and sulci is shown among four mammals—a goat, a cat, an indri lemur, and a chimpanzee—in Figure 19-18.

The medial, hippocampal cortex (Fig. 19-11) includes the **dentate gyrus**, the **hippocampus**, which is also referred to as **Ammon's horn**, and the **subicular cortices**. The hippocampal formation was divided into regions designated CA₁ to CA₄ (CA for *cornu Ammonis*, which is "Ammon's horn" in Latin—see Box 30-2) by Lorente de No in the early part of this

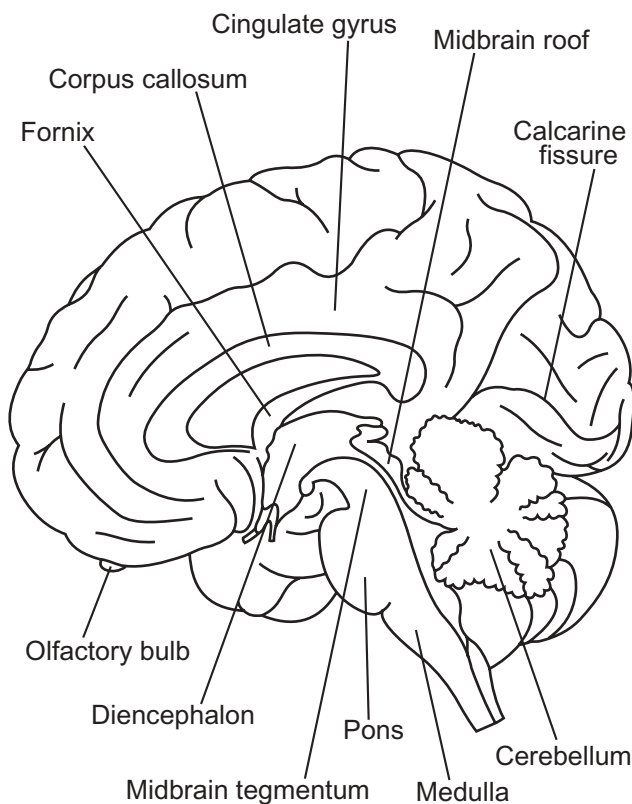


FIGURE 19-16. Medial midsagittal view of the brain of a primate (*Homo sapiens*), with rostral toward the left. Adapted from Nieuwenhuys et al. (1978) and used with kind permission of Springer Science and Business Media.

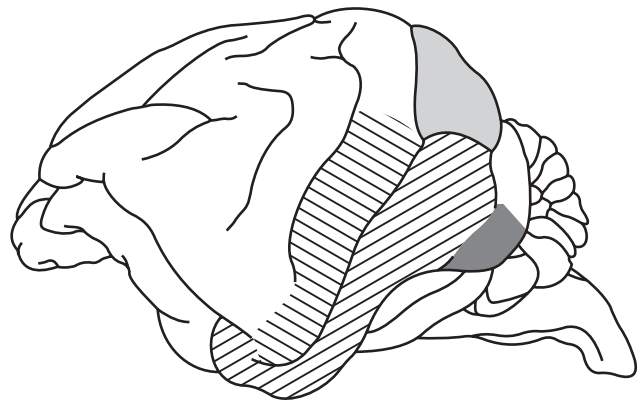


FIGURE 19-17. Lateral view of the brain of an echidna (*Tachyglossus aculeatus*), with rostral toward the left. The area of motor cortex is indicated by diagonal lines toward the upper left and is rostral to that of somatosensory cortex, indicated by diagonal lines toward the upper right. Visual cortex is the more lightly shaded area dorsal to somatosensory cortex, and auditory cortex is the more darkly shaded area caudal to somatosensory cortex. Adapted from Rowe (1990) and used with kind permission of Springer Science and Business Media.

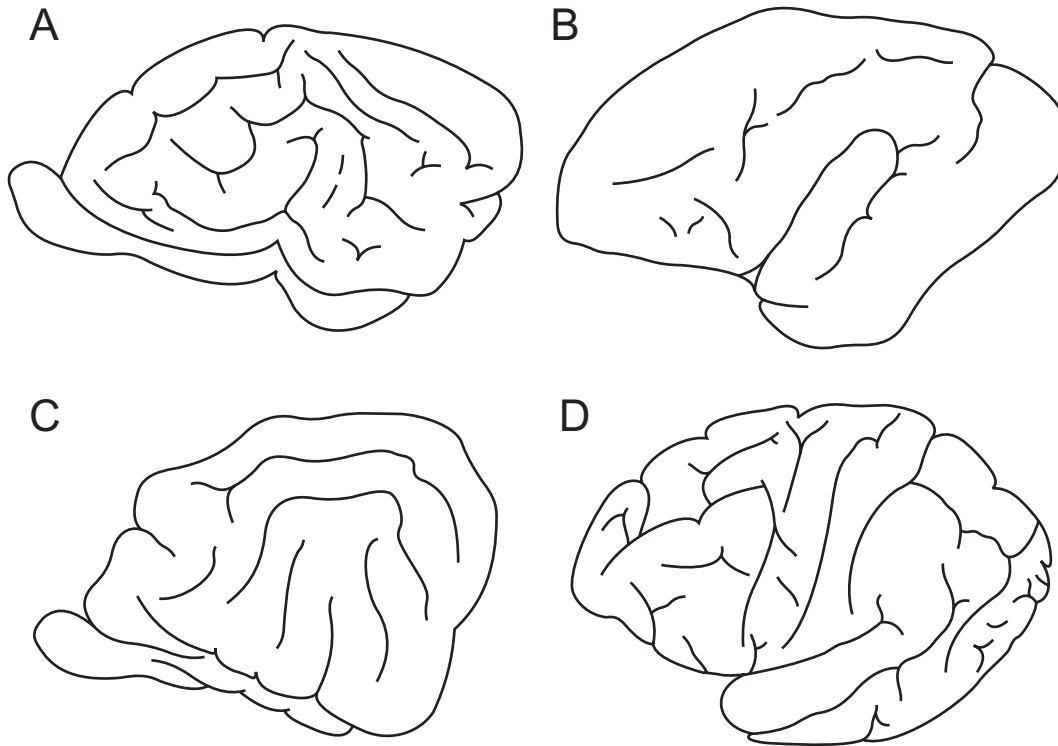


FIGURE 19-18. Lateral views of the cerebral hemispheres in a goat (A), an indri lemur (B), a domestic cat (C), and a chimpanzee (D). Rostral is toward the left. Adapted from Ariëns Kappers et al. (1967).

century, and these designations are frequently used in the literature. The subicular cortices border entorhinal cortex, which in turn borders the piriform cortex. The **cingulate gyrus** (Figs. 19-16 and 19-19), a part of the neocortex on the medial surface of the cerebral hemisphere, is connectionally and functionally included in the limbic system. The subicular cortices and entorhinal cortex are transitional cortices between the neocortex and the three-layered hippocampal and olfactory cortices. The neocortex is expanded to such a degree in many mammals that parts of the hippocampal formation and the olfactory cortices come into contact with each other ventrally in the temporal lobe.

The lateral region of the cerebral hemisphere comprises several regions (Fig. 19-20). The **piriform cortex**, which is one of the primary targets of the olfactory bulb, is a three-layered cortex that extends ventrolaterally from the lateral part of the neocortex, their dividing line marked by the rhinal fissure. Deep to the lateral part of neocortex (insular neocortex) and the piriform cortex are two structures of the deeper part of the cortical mantle, the **claustrum** and the **endopiriform nucleus**, respectively. Finally, the **amygdala**, comprising both cortical and nuclear parts, forms the most lateral part of the pallium and includes striatal components as well.

The claustrum (Figs. 19-11, 19-19, and 19-20) is formed by a relatively thin layer of gray matter that lies between the pallial cortex of the temporal lobe and the putamen. It can also be referred to as the insular claustrum or the claustrum proper to distinguish it from the more ventrolaterally lying endopiriform nucleus. Based on developmental evidence, histochemistry,

and other features, both the claustrum and the endopiriform nucleus recently have been recognized as pallial components rather than subpallial ones. These structures are present in eutherian and marsupial mammals. In monotremes, the claustrum and endopiriform nucleus are either absent or very reduced. They are not identifiable with any certainty in the platypus, and whether they are present in the echidna remains a matter of controversy. Likewise, homologues of these structures have yet to be identified definitively in any nonmammalian vertebrate.

In terms of its connections, the claustrum is primarily involved with the neocortex. It has extensive reciprocal connections with all neocortical areas, including the primary and association sensory cortices of the visual, auditory, and somatosensory systems and the motor and association cortices of the frontal lobe. The claustrum may thus play an integrative role in cortical functions. In addition, the claustrum receives afferent input from subcortical structures, including the hypothalamus and a group of widely projecting nuclei in the dorsal thalamus called the intralaminar nuclei.

From rostral to caudal, the olfactory cortices, which receive direct input from the olfactory bulb, comprise the **anterior olfactory nucleus**, **piriform cortex**, the **olfactory tubercle** (to which we will return below), a number of amygdalar sites, including a laminated part of it called the **cortical amygdala**, and the **entorhinal cortex**. Additionally, the accessory olfactory bulb, where present, projects to a part of the cortical amygdala and to the **medial amygdaloid nucleus**.

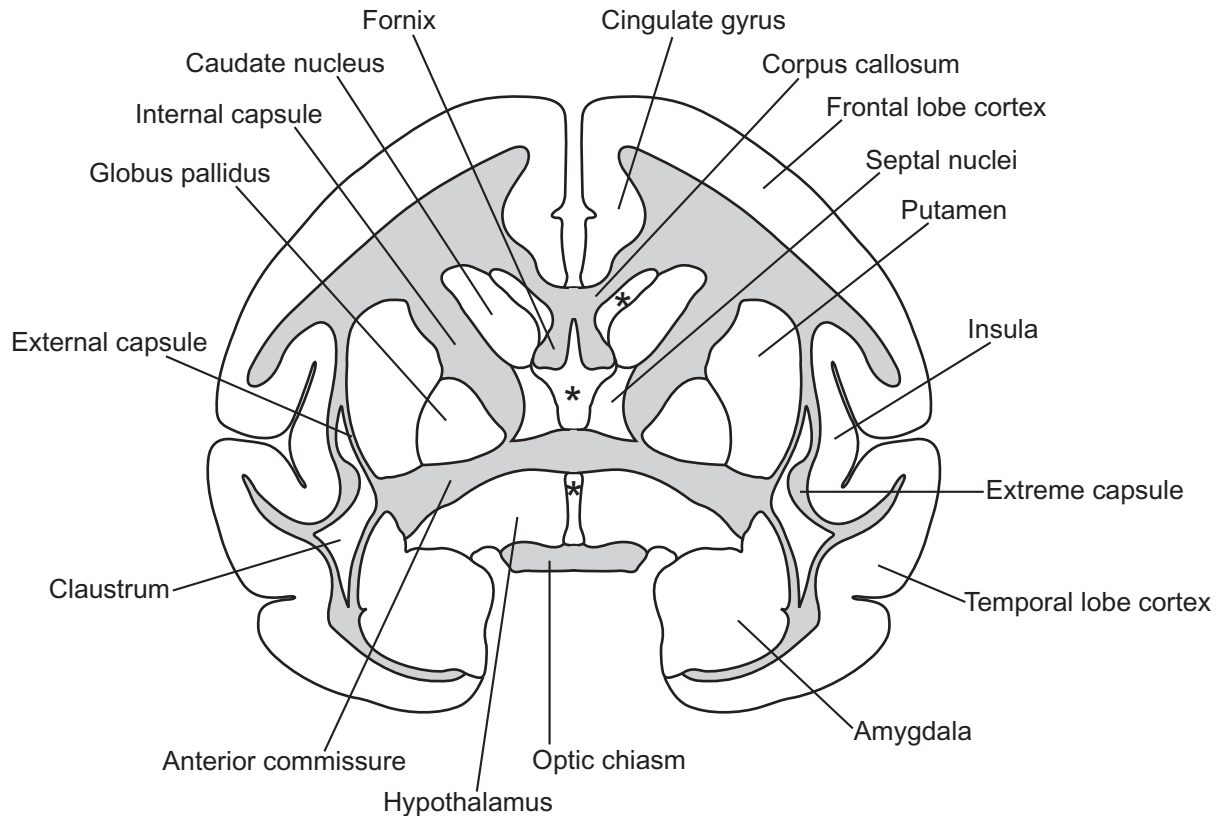


FIGURE 19-19. Drawing of a transverse hemisection through the right forebrain of a squirrel monkey (*Saimiri sciureus*). The major white matter fiber tracts are shaded. Asterisks indicate ventricular spaces. Adapted from Gergan and MacLean (1962).

The amygdala (Figs. 19-11 and 19-19) traditionally has been regarded as part of the limbic system. It comprises a collection of rather diverse nuclei as well as overlying cortical areas. Most of its components are of pallial origin. In 1998, Larry Swanson and Gorica Petrovich proposed that the amygdala actually consists of four major and quite distinct functional units (Fig. 19-20). Rather than regarding the “amygdala” as a single, highly interrelated entity, it is much more readily understood in these terms.

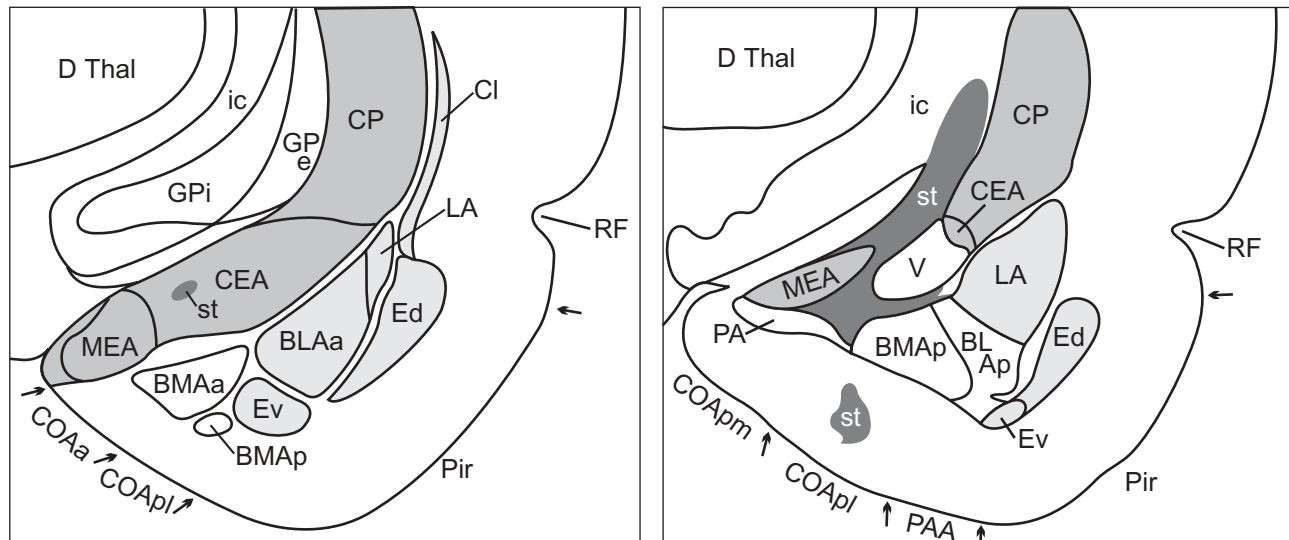
Swanson and Petrovich identified four major groups of nuclei, two of which are associated with the accessory and main olfactory systems. These two groups each include portions of the cortical amygdala and of a posterior amygdalar nucleus. The accessory olfactory amygdalar division also includes the medial amygdaloid nucleus, which is a subpallial, striatal component. The medial and some of the other olfactory-related parts of the amygdala project to the hypothalamus via a tract called the **stria terminalis** (Fig. 19-20) and to the **bed nuclei of the stria terminalis**, subpallial sets of neurons that lie along this pathway that also project to the hypothalamus. Due to the close relationship of the main and accessory olfactory amygdalar nuclei to the olfactory system, these nuclei will be discussed in Chapter 29.

The third division of the amygdala is related to the autonomic nervous system and constitutes a subpallial, striatal component, the **central amygdaloid nucleus**, which is

connected with the bed nuclei of the stria terminalis and the hypothalamus, as well as with the autonomic nervous system via structures within the brainstem. The medial and central amygdalar nuclei are actually components of the striatum, being a ventral continuation of the caudate-putamen. Thus, they will be discussed in Chapter 24. Along with the bed nuclei of the stria terminalis, they comprise the major part of a functional group referred to as the **extended amygdala**, which is discussed further below.

The fourth division of the amygdala can be referred to as the **frontotemporal amygdala**, since it is heavily interconnected with frontal and temporal neocortical regions. This group comprises the **lateral** and the **anterior basolateral amygdaloid nuclei**. The former receives direct sensory input from dorsal thalamic nuclei. The frontotemporal division of the amygdala will be discussed in Chapter 25.

Figure 19-20 shows two levels through the amygdala that include most of the nuclei categorized into the four groups. These nuclei are listed in the lower part of the figure. Additionally, the close relationship of the frontotemporal amygdala to the claustrum and endopiriform nuclei is indicated in the drawings by their shared light shading, and in the table, all of these nuclei are also grouped as the **claustramygdalar complex**. Likewise, the close relationship of the medial and central amygdalar nuclei to the caudate-putamen is indicated by their shared medium shading in both the drawings and the table.



AMYGDALA	1. Main Olfactory Amygdala	COAa (cortical nucleus amygdala, anterior part)	Olfactory Pallial Amygdala
		PAA (piriform-amygdalar area)	
		TR (postpiriform transition area)	
		COApI (cortical nucleus amygdala, posterior part, lateral zone)	
		BMAa (basomedial nucleus amygdala, anterior part)	
		BMAp (basomedial nucleus amygdala, posterior part)	
		BLAp (basolateral nucleus amygdala, posterior part)	
	2. Accessory Olfactory Amygdala	PA (posterior nucleus amygdala)	Striatal Amygdala
		COApm (cortical nucleus amygdala, posterior part, medial zone)	
		MEA (medial nucleus amygdala)	
	3. Autonomic Amygdala	CEA (central nucleus amygdala)	Claustro-amygdalar Complex (Pallial)
	4. Frontotemporal Amygdala	BLAa (basolateral nucleus amygdala, anterior part)	
		LA (lateral nucleus amygdala)	
Claustrum-endopiriform Formation		Ed (Endopiriform nucleus, dorsal part)	
		Ev (Endopiriform nucleus, ventral part)	
		Cl (Claustrum, i.e., claustrum proper or insular claustrum)	

FIGURE 19-20. Drawings of transverse sections, with the more rostral one on the left, through the temporal lobe of the rat showing most of the components of the amygdala. The table lists these nuclei and cortical areas in terms of the four major functional groups identified by Swanson and Petrovich (1998) from whom this figure is adapted. Abbreviations not included in table: D Thal, dorsal thalamus; GPe, external segment of globus pallidus; GPi, internal segment of globus pallidus; ic, internal capsule; Pir, piriform cortex; RF, rhinal fissure; st, stria terminalis; V, lateral ventricle. The shadings in the drawings of darker gray and lighter gray for striatal and claustroramygdalar components, respectively, are correspondingly applied in the table. Used with permission of Elsevier.

Many fiber tracts are present in the telencephalon. For orientation, several need to be introduced here. In mammals, the largest pathway connecting the telencephalon with the rest of the brain is a collection of afferent and efferent fibers that, in the telencephalon, is called the **internal capsule** (Figs. 19-11 and 19-19). The internal capsule is a clearly demarcated fiber bundle as it passes through the region of the striatum. In fact, it is the fibers of the internal capsule that form the “stripes” of the striatum, giving it its name. The fibers in the internal capsule continue caudally through the brainstem, where they are referred to as the **pes pedunculi** (see Fig. 17-12). Superficial to the internal capsule are two other, smaller fiber bundles: the **external capsule** and the **extreme capsule** (Fig. 19-19), which lie on either side of the claustrum.

In all vertebrates, some fiber bundles are present in the telencephalon, as in the rest of the brain, that connect the two sides with each other. In mammals, the **hippocampal commissure** reciprocally interconnects the hippocampal formations, including its transitional cortices. The **anterior commissure** (Fig. 19-19) reciprocally interconnects some of the more ventral and lateral parts of the telencephalon, including the olfactory cortices. In monotremes and marsupials, the anterior commissure also carries all of the commissural fibers that arise from neocortex, while in eutherian (placental) mammals, the anterior commissure carries only some of the neocortical commissural fibers, particularly those from the temporal neocortex.

Some marsupials and all eutherian mammals have one additional commissural system that is unique among the vertebrate radiations. This unique commissural bundle is very large and is called the **corpus callosum** (Figs. 19-16 and 19-19). Its fibers reciprocally connect wide areas of the neocortex with their respective, homotopic (mirror-image) areas in the contralateral neocortex. The corpus callosum also carries commissural fibers from transitional cortices and the striatum. Several theories have been advanced concerning the evolution of this commissure, including derivation from either the anterior commissure or the hippocampal commissure, but consensus has not been achieved.

The Telencephalic Pallium of Nonmammalian Amniotes

As in mammals, the telencephalic pallium in sauropsids (reptiles and birds) is divisible into three main parts—medial, dorsal, and lateral. In reptiles, neurons in the olfactory (lateral) pallium, part of the dorsal pallium, and the limbic (medial) parts of the pallium are migrated away from the periventricular surface so that a three-layered cortex—of two relatively cell-free zones with an intermediate cell-dense layer—is formed. The three-layered part of the dorsal pallium, the **dorsal cortex** (Fig. 19-21), receives ascending visual and somatosensory projections from nuclei in the dorsal thalamus that are in receipt of lemniscal pathways. As in most anamniote vertebrates, the surface of the cerebral hemisphere is relatively smooth (Fig. 19-22).

A second, substantial part of the pallium is formed by a large area, the **anterior dorsal ventricular ridge** (ADVR, Fig. 19-21), which is a medially expanded bulge deep to the cortices. The anterior dorsal ventricular ridge (sometimes referred

to simply as the dorsal ventricular ridge) receives ascending visual, auditory, and somatosensory projections from dorsal thalamic nuclei that receive their predominant input from the midbrain tectum (the colliculi of mammals). Whether the dorsal ventricular ridge should be regarded as part of the dorsal pallium or not is currently unresolved. It may arise as a component of the lateral pallium, which in addition to the olfactory cortex also gives rise to parts of the amygdala and claustrum-endopiriform formation in mammals, and/or of a recently described additional pallial moiety, the ventral pallium. The latter gives rise to other parts of the pallial amygdala and claustrum-endopiriform formation in mammals. As will be discussed further in Chapter 25, the relationship of the sauropsid DVR to pallial amygdalar and/or claustrum-endopiriform components of mammals and/or to the more lateral, collothalamus-recipient part of neocortex remains a matter of debate.

The medial pallium, which comprises the **medial** and **dorsomedial cortices** (Fig. 19-21), is thought to be homologous, at least as a field, to the medial (limbic) pallium of mammals. The medial cortex of reptiles has been homologized to the dentate gyrus as a specific set of neurons and the dorsomedial cortex likewise to Ammon's horn, although some data suggest a less discrete correspondence. In birds, some research has indicated that the topologic order is reversed, with Ammon's horn lying ventral (medial) to the dentate gyrus, while other recent findings indicate that the topologic order is the same as in other amniotes, with the dentate gyrus homologue situated most ventrally (medially).

Some workers have proposed that the entire dorsal cortex of reptiles is homologous to transitional cortices, particularly the subiculum, rather than to any part of mammalian neocortex. Others have hypothesized that the dorsal cortex and the anterior dorsal ventricular ridge are homologous, as a field, to the neocortex (neocortex) of mammals. Still others have made a case for the hypothesis that the anterior dorsal ventricular ridge and those parts of the neocortex with similar ascending connections are independently evolved and therefore homoplaseous.

Whatever the relationship of the dorsal ventricular ridge to pallial components in mammals, two major divisions of the nonlimbic, nonolfactory pallial areas can be identified for all amniotes that correspond to the divisions of the dorsal thalamus. As noted above, the dorsal thalamus can be divided into a predominantly lemniscal-recipient lemnothalamus and a predominantly midbrain roof-recipient collothalamus. Similarly, there are two divisions of the dorsal pallium:

- A medial, **lemnothalamic pallium**, or **lemnopallium**, which receives its predominant dorsal thalamic input from the lemnothalamus.
- A lateral, **collothalamic pallium**, or **collopallium**, which receives its predominant dorsal thalamic input from the collothalamus.

This hypothesis holds that the dorsal (or general) cortex of reptiles and the Wulst of birds (discussed below) are homologous to the lemnopallial part of the neocortex (i.e., those parts that receive projections from the lemnothalamus) and the subicular cortices of mammals. Likewise, the anterior dorsal ventricular ridge is homologous to part or all of the collopall-

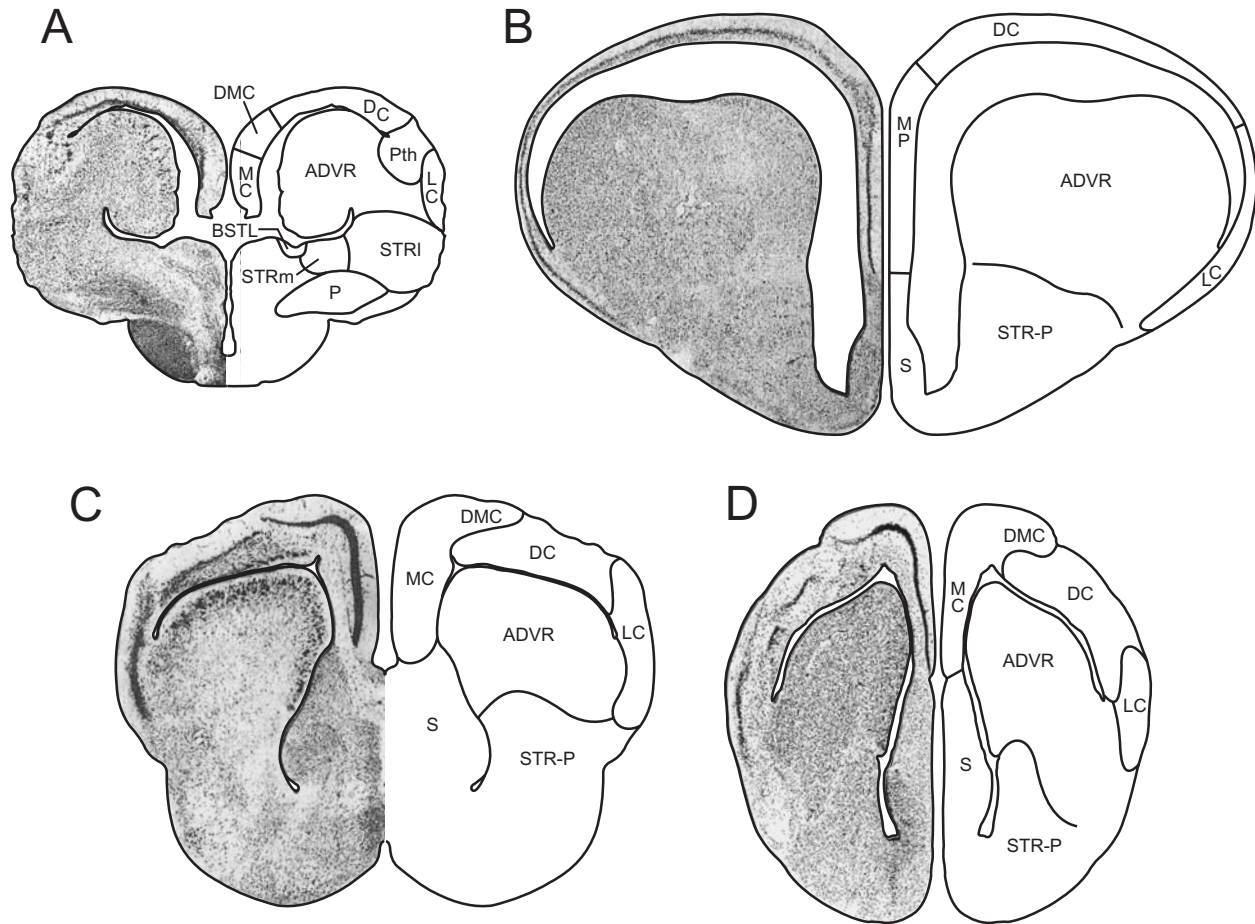


FIGURE 19-21. Transverse hemisections with mirror-image drawings through the telencephalon of: a turtle (*Pseudemys scripta*) (A), a crocodile (*Alligator mississippiensis*) (B), a Type I lizard (*Gekko gekko*) (C), and a Type II lizard (*Tupinambis nigropunctatus*) (D). Abbreviations: ADVR, anterior dorsal ventricular ridge; BSTL, lateral bed nucleus of stria terminalis; DC, dorsal cortex; DMC, dorsomedial cortex; LC, lateral cortex; MC, medial cortex; MP, medial pallium; P, pallidum; Pth, pallial thickening; S, septal nuclei; STRl, lateral part of dorsal striatum; STRm, medial part of dorsal striatum; STR-P, dorsal striatopallidal region. Adapted from Ulinski (1983) with modifications in A from Powers et al. (2003) and used with permission of John Wiley & Sons.

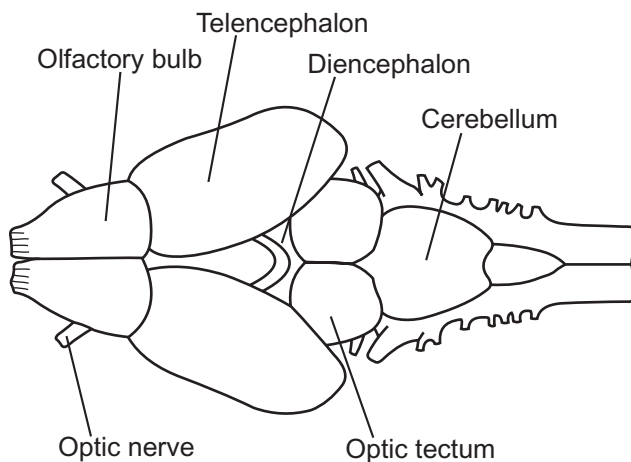


FIGURE 19-22. Dorsal view of the brain of a turtle (*Chrysemys picta*). Adapted from Northcutt (1979) and used with permission of The University of Chicago Press.

lium of mammals (i.e., those parts of neocortex and/or pallial amygdala that receive projections from the collothalamus). Some features, such as the particular morphology of the dorsal ventricular ridge versus that of neocortex or amygdala and particular cell phenotypes within the dorsal pallia of mammals and of some nonmammalian amniotes, were evolved independently within the areas homologous as fields.

The **lateral cortex** (Fig. 19-21) in reptiles is thought to be homologous to at least part of the olfactory cortex of mammals. It is in receipt of direct olfactory projections. In the caudal part of the dorsal ventricular ridge in lizards and snakes is a large nucleus, **nucleus sphericus**, which consists of a laminar cell layer and a central neuropil and receives an input from the accessory olfactory bulb. Nucleus sphericus is homologous to the pallial components of the accessory olfactory division of the amygdala of mammals. Other amygdalar nuclei are also present, bordering the more rostral part of nucleus sphericus in the caudal part of the dorsal ventricular ridge.

In birds, as in reptiles, the pallium consists of the medial (limbic) pallium (Table 19-6), piriform (olfactory) cortex, and two other main regions—the **Wulst** and the **dorsal ventricular ridge (DVR)**. “Wulst” is German for swelling, bulge, or hump, and the avian Wulst comprises an expanded part of the pallium that lies in the rostral part of the telencephalon and forms a bulge on the surface of the telencephalic hemisphere (Fig. 19-23). Its several cytoarchitectonically distinct regions

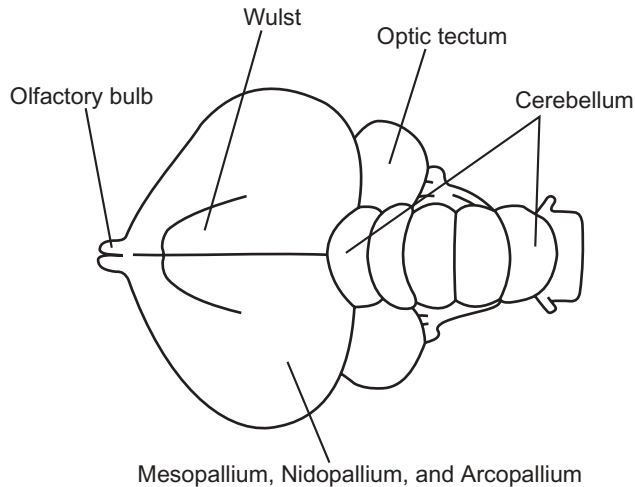


FIGURE 19-23. Dorsal view of the brain of a pigeon (*Columba livia*). Adapted from Northcutt (1979) and used with permission of The University of Chicago Press.

are collectively known as the **hyperpallium** (Fig. 19-24; Table 19-2), which corresponds to at least part of the dorsal cortex of reptiles. The hyperpallium receives ascending visual and somatosensory projections. It also gives rise to a major descending motor pathway to the brainstem and spinal cord. The avian dorsal ventricular ridge comprises several regions (Fig. 19-24), the major ones being the **mesopallium** (Table 19-3), **nidopallium** (Table 19-4), and **arcopallium** (Table 19-5). The mesopallium was formerly grouped with the hyperpallium, at least in terms of its nomenclature, but is now recognized as the dorsal-most component of the DVR. The nidopallium has subdivisions, including areas that receive visual [**entopallium** (Fig. 19-24)], auditory (**Area L pallii**), and trigeminal (**nucleus basorostralis pallii**) inputs. The arcopallium contains multiple subdivisions as well, at least some of which are homologous to components of the mammalian amygdala.

Although the Wulst and dorsal ventricular ridge of birds and the homologous regions in reptiles may contain regions that are homologous to respective regions of mammalian neocortex as part or all of various fields, as discussed above, some specific features of given pallial areas have been independently derived in different lineages. Two specific phenotypes of pallial neurons, as defined by their neurotransmitter or neuroactive substance profile, appear to be present only in mammals, whereas a third appears to have been evolved independently in both mammals and birds.

A variety of neuroactive substances characterize neurons in the infragranular layers (V and VI) of mammalian neocortex and are also present in the dorsal pallium of nonmammalian amniotes. In contrast, three substances—cholecystokinin-8

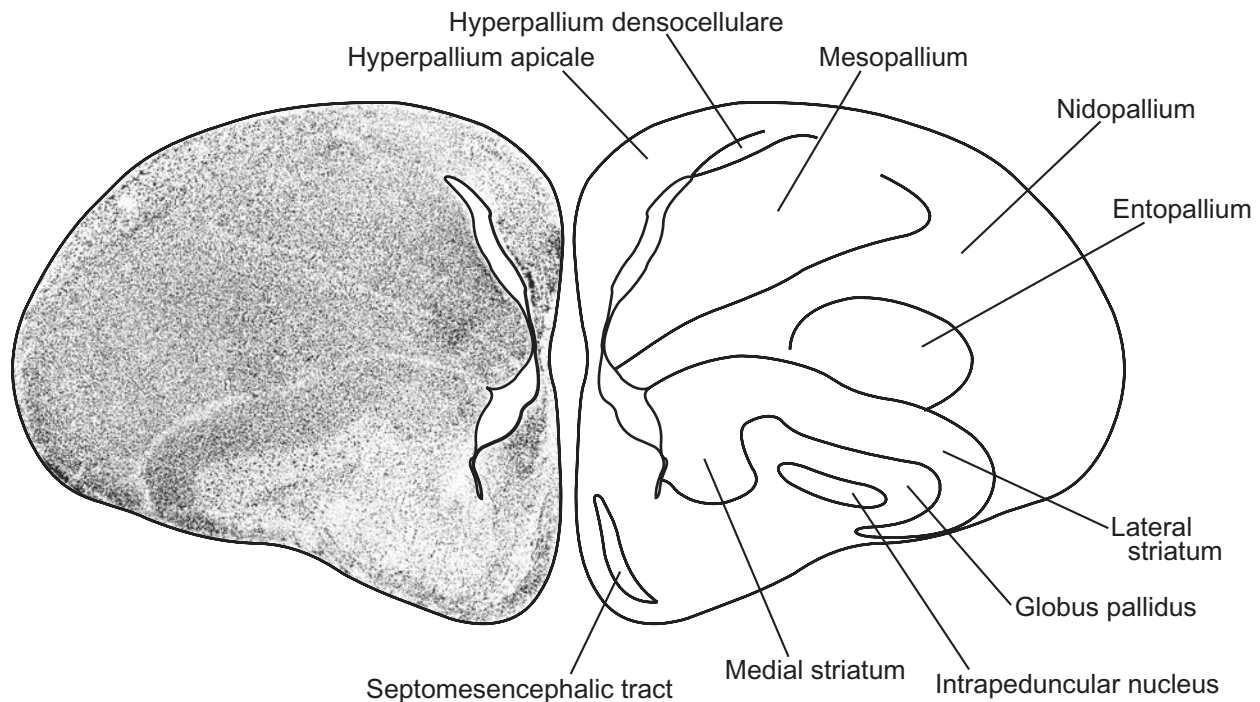


FIGURE 19-24. Transverse hemisection with mirror-image drawing through the telencephalon of a pigeon (*Columba livia*). Adapted from Karten and Hodos (1967), with nomenclature based on Reiner et al. (2004) and used with permission of The Johns Hopkins University Press.

(CCK8), vasoactive intestinal polypeptide (VIP), and choline acetyltransferase (CHAT, an indicator of the presence of acetylcholine)—are specific for the neurons in layers II, III, and IV of mammalian neocortex. Neurons containing VIP or CHAT have not been found in the dorsal pallium of nonmammalian amniotes, while neurons containing CCK8 occur only in birds.

In mammals, neurons in layers II and III give rise to corticocortical connections, both ipsilaterally and interhemispherically, and granule cells in layer IV, which receive the major part of ascending dorsal thalamic sensory projections, are present in prodigious quantity. Some interhemispheric connections are present in reptiles, and some evidence of ipsilateral corticocortical connections exists, but such intercortical connections are sparse in nonmammalian amniotes compared with mammals. Only in the dorsal pallium of birds do granule-like cells appear to exist in quantity.

Thus, some sets of neurons with specific neuroactive substances and connections, particularly some of those within layers II–IV of neocortex, may not have been present in the dorsal pallium of the common amniote ancestral stock. Because these regions are considered to be homologous as fields, however, the presence of some specific apomorphic traits in given lineages is not an unlikely finding. The neuroactive substance or transmitter phenotype of a given neuron can be influenced during development by a variety of epigenetic factors. The presence of novel phenotypes of dorsal pallial neurons could thus occur as a result of minor shifts in the developmental process, and selective pressures favoring their maintenance would result in the establishment of such developmental shifts, themselves under genetic control, in the population.

As discussed above, only therian mammals have a massive interhemispheric commissure, the corpus callosum. An anterior commissure that carries olfactory and some neocortical interhemispheric fibers and a hippocampal commissure are also present in mammals. The best developed commissure in nonmammalian amniotes, the **anterior pallial commissure**, appears to correspond to the hippocampal commissure of mammals. It crosses the midline at the base of the medial cortex and primarily interconnects the medial pallial regions but has also been found to carry a minor component of dorsal pallial interhemispheric fibers, at least in some reptiles. A more caudal and less well developed commissure, called the posterior pallial commissure or the anterior commissure, carries interhemispheric connections of the more caudal pallial regions. A large collection of ascending and descending fibers, consisting of the **medial and lateral forebrain bundles** (Fig. 19-5), is also present in the forebrain of nonmammalian amniotes, corresponding to the internal capsule/pes peduncular system and other projection systems of the forebrain in mammals. The lateral forebrain bundle is frequently divided into two parts called the **dorsal** and **ventral peduncles**.

THE TELENCEPHALON: SUBPALLIUM

The **striatopallidal complexes** and the **septum** are two major components present in the ventral part of the telencephalon. The striatopallidal complexes lie ventrolaterally; they

are concerned with motor functions and are also interconnected with the limbic system, whereas the septum lies ventromedially and is functionally and connectionally related to the limbic system. Additional subpallial components lie ventral to the striatopallidal complexes and the septum.

The Ventrolateral Telencephalon of Anamniotes

The ventrolateral part of the telencephalon contains a number of structures in all vertebrate groups. A variety of terms have been used for this region in general and also for some of its specific components, including corpus striatum, dorsal striatum, and so on. Striatum simply means “striped” and refers to the appearance of two of the nuclei (the caudate nucleus and putamen) in the ventrolateral telencephalon in mammals that are crossed by a fiber pathway (the internal capsule), which therefore have a striped appearance. In current usage, use of the word “striatum” should mainly be restricted to the dorsal striatum and ventral striatum components of the striatopallidal complexes, as listed below in the section on mammals. The ventrolateral telencephalon also includes the target nuclei of the striatum, which are called pallidum, and several other nuclear groups as well.

Dorsal and ventral divisions of the striatum, the latter identified as nucleus accumbens, have been identified in amphibians, as has an anterior (or rostral) entopeduncular nucleus, which is thought to be pallidal in nature. Similar regions are present in other anamniotes. One nucleus present in cartilaginous fishes—**area periventricularis ventrolateralis**—may correspond to the dorsal striatum of mammals (see below), and another nucleus—**nucleus superficialis basalis**—may correspond to the mammalian ventral striatum (see below). In ray-finned fishes with everted pallia, the subpallial relationships are at least partially conserved in comparison to those in other vertebrates. A nucleus called the ventral nucleus of area ventralis (Vv) may be comparable to the septal nuclei but may also contain ventral striatal components; it lies ventral to the region comparable to the dorsal striatum.

The Ventrolateral Telencephalon of Mammals

In mammals, the terminology used for the subpallial structures in the ventrolateral telencephalon needs to be reviewed before we discuss the structures themselves and their connections. Various nuclei have been referred to as the **basal ganglia**, in which three nuclei—the **caudate nucleus**, **putamen**, and **globus pallidus**—are most frequently included. The substantia nigra of the mesencephalon and other related structures are sometimes included in this term as well. The term basal ganglia is now waning in popularity in favor of newer terms that reflect a better understanding of the connections and neurotransmitters of the various cell groups. The ventrolateral telencephalon (Table 19-7) of mammals can be divided into three major parts:

- The **striatopallidal complexes**.
- A ventral region referred to as the **extended amygdala**.
- Groups of large, cholinergic neurons, including **nucleus basalis of Meynert**.

TABLE 19-7. Ventrolateral Telencephalon of Mammals

(1) Striatopallidal Complexes	Dorsal striatopallidal complex	Dorsal striatum	Caudate nucleus		Corpus striatum
			Putamen	Lentiform nucleus	
		Dorsal pallidum	Globus pallidus		
	Ventral striatopallidal complex	Ventral striatum	Olfactory tubercle and nucleus accumbens		
		Ventral pallidum	Ventral pallidum (in rostral substantia innominata)		
(2) Extended Amygdala	Central amygdaloid nucleus, cell columns in the anterodorsal part of the sublenticular substantia innominata, and the lateral bed nucleus of the stria terminalis				
	Medial amygdaloid nucleus, cell columns in the posteroventral part of the sublenticular substantia innominata, and the medial bed nucleus of the stria terminalis				
(3) Nucleus Basalis and Other Cholinergic Cell Groups	Nucleus basalis of Meynert, the medial septal nucleus, and the vertical and horizontal limbs of the nucleus of the diagonal band of Broca				

The Striatopallidal Complexes. The striatopallidal complexes have two divisions: a dorsal division, composed of the **dorsal striatum** and the **dorsal pallidum**, and a ventral division, composed of the **ventral striatum** and the **ventral pallidum**. The two complexes have similar circuitry. The striatal components of each complex receive major inputs from ascending dopaminergic systems of the midbrain and from the neocortex. The striatal components contain inhibitory, GABAergic neurons that project to the pallidal components of each complex. The pallidal components also contain GABAergic neurons, and some of these neurons project in turn into the dorsal thalamus, particularly to nuclei that project back to motor-related regions of neocortex. Activity of the pallidal neurons inhibits thalamic activity, thereby decreasing the excitatory input of thalamus to neocortex and thus inhibiting the initiation of movements. Conversely, inhibition of the pallidal neurons allows greater thalamic activity and thus fosters the initiation of movements. This circuitry will be discussed in detail in Chapter 24.

The dorsal striatum comprises the caudate nucleus and the putamen (Fig. 19-19), which are in reality a single nucleus, artificially divided by fibers of the internal capsule at this level. The name caudate means “tail,” in reference to the “C”-shaped caudal extension of the caudate nucleus as seen in the sagittal plane (Fig. 19-25). The globus pallidus (Fig. 19-19) forms the dorsal pallidum and lies ventromedial to the caudate nucleus and putamen. Due to their combined shape in transverse section, the putamen and globus pallidus sometimes are referred to as the **lentiform nucleus**, although there is no connectional or functional basis for recognizing them as a single nucleus. The term lentiform nucleus is useful, however, as it is sometimes referred to as an anatomical landmark in relation to other structures. The caudate-putamen and the globus pallidus are sometimes referred to as the corpus striatum (striped body).

In mammals, the globus pallidus generally has two segments. In primates, these segments are called **external** and **internal**. In nonprimate mammals, the external segment is

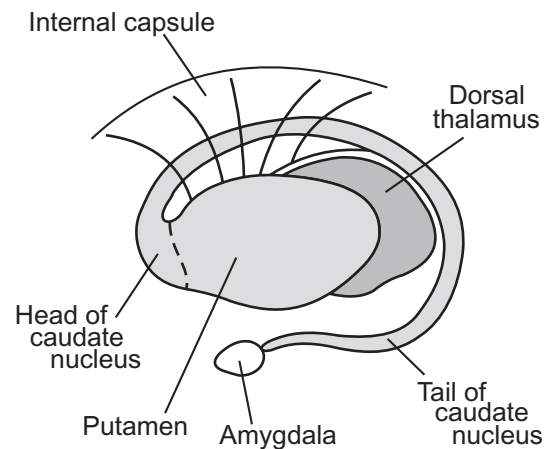


FIGURE 19-25. Reconstruction of a lateral view of the caudate nucleus and putamen (lighter shading), with part of the dorsal thalamus (darker shading) medial to the putamen. Rostral is toward the left. The fibers of the internal capsule are indicated by curved lines as they pass ventrocaudally between the caudate nucleus and the putamen.

simply called the globus pallidus, and the internal segment is called either the internal segment or the **entopeduncular nucleus**. This entopeduncular nucleus is the homologue of a cell group most often identified as the rostral entopeduncular nucleus in nonmammalian vertebrates.

The ventral striatopallidal complex comprises two structures that form the ventral striatum—the **olfactory tubercle** and **nucleus accumbens**—and the ventral pallidum. The olfactory tubercle is anatomically within the olfactory cortex (as mentioned above) but is now regarded as part of the ventral striatum (Fig. 19-26). Deep to the olfactory tubercle and adjoining the ventromedial border of the caudate-putamen is the nucleus accumbens, which can be divided into shell and core regions (Fig. 19-26). This nucleus was originally named nucleus

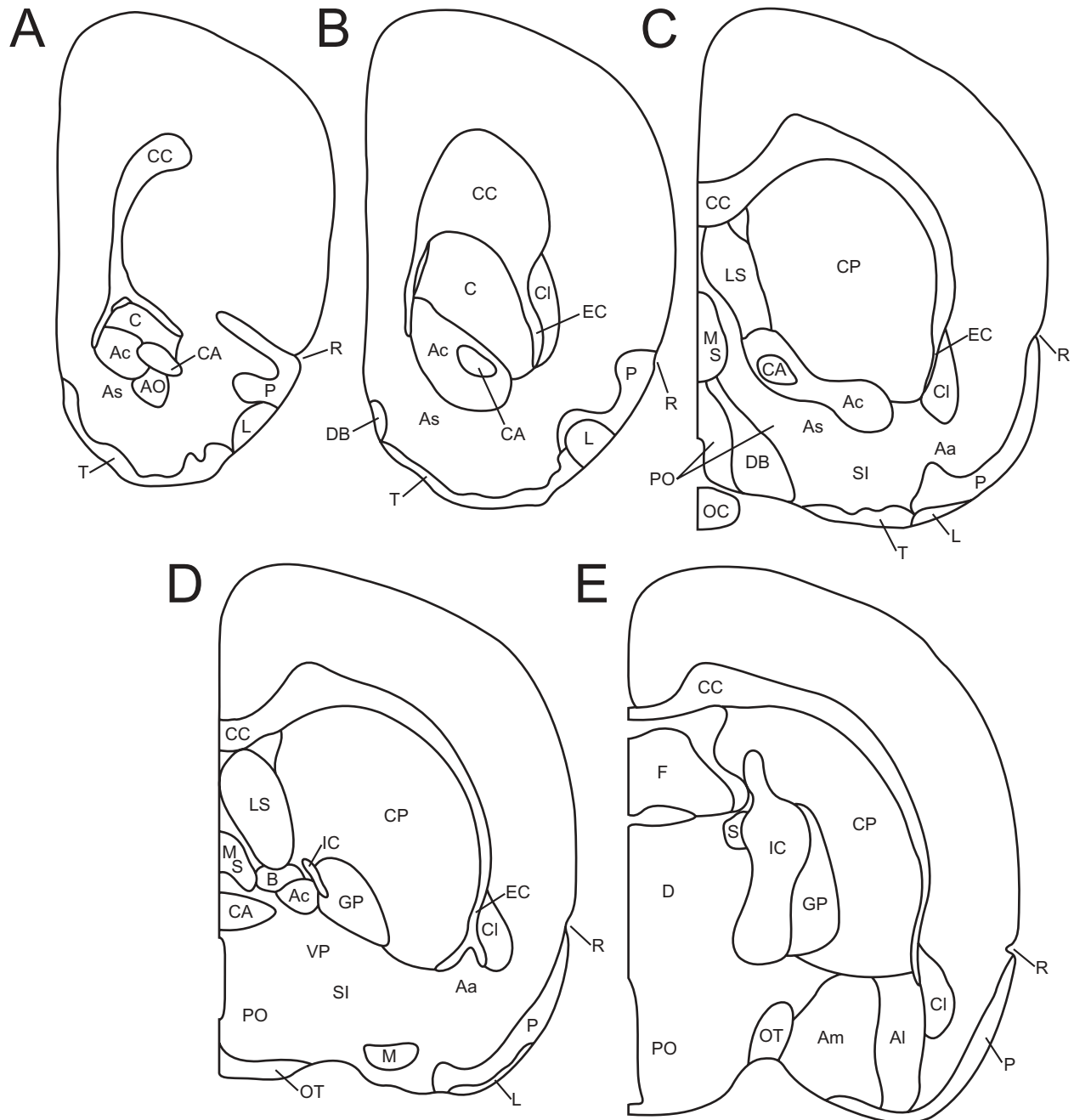


FIGURE 19-26. Drawings of a series of transverse hemisections through the right telencephalon of a rat, with A most rostral and E most caudal. Abbreviations: Aa, anterior amygdalar area; Ac, core of nucleus accumbens; Al, basolateral amygdala; Am, centromedial amygdala; Ao, anterior olfactory nucleus; As, shell of nucleus accumbens; B, bed nucleus of stria terminalis; C, caudate nucleus; CA, anterior commissure; CC, corpus callosum; Cl, claustrum; CP, caudate-putamen; D, diencephalon; DB, nucleus of the diagonal band; EC, external capsule; F, fornix; GP, globus pallidus; IC, internal capsule; L, lateral olfactory tract; LS, lateral septum; M, nucleus basalis (magnocellular corticopetal cell complex); MS, medial septum; OC, optic chiasm; OT, optic tract; P, piriform cortex; PO, preoptic area; R, rhinal sulcus; S, stria terminalis; SI, substantia innominata; T, olfactory tubercle; VP, ventral pallidum. Adapted from Pelligrino et al. (1979) and used with kind permission of Springer Science and Business Media.

accumbens septi; however, because it now is regarded as part of the striatopallidal complex rather than part of the septum, the “septi” has been dropped from its name in common usage. The core of nucleus accumbens surrounds the anterior commissure and is continuous cytoarchitectonically with the caudate-putamen. A distinct shell region encircles the core, except at the rostral pole where separate shell and core regions cannot be distinguished. In macrosmatic animals (those in which the sense of smell is well developed), cell bridges exist between the olfactory tubercle and nucleus accumbens.

Ventral to the globus pallidus is a region that was not named when it was first described and has thus become known as the **substantia innominata**, meaning the “unnamed substance” (Fig. 19-26). Several different populations of neurons are present within the substantia innominata, one of which is the ventral pallidum. The neurons of the ventral pallidum resemble those of the dorsal pallidum, that is, the globus pallidus; however, rather than being grouped within an obviously bounded nucleus, they are scattered within the substantia innominata, particularly in its more rostral part. The substantia innominata extends rostrocaudally for some distance; the part of it that lies ventral to the lentiform nucleus (the globus pallidus and putamen) is referred to as the sublentiform substantia innominata. The cell population of the ventral pallidum extends rostroventrally between the globus pallidus and nucleus accumbens dorsally and the olfactory tubercle ventrally (Fig. 19-26).

The Extended Amygdala of Mammals. The second major part of the ventrolateral forebrain is the extended amygdala. The extended amygdala has two major divisions—the first comprising the central nucleus of the amygdala, cell columns present in part of the sublentiform substantia innominata, and the lateral bed nucleus of the stria terminalis, and the second comprising the medial nucleus of the amygdala, cell columns in a more posterior and ventral part of the sublentiform substantia innominata, and the medial bed nucleus of the stria terminalis.

The bed nuclei of the stria terminalis, a tract that connects the hypothalamus with parts of the amygdala as discussed above, lie between the septal region and nucleus accumbens. The area of the extended amygdala, which extends caudally from the major part of nucleus accumbens, is shown in Figure 19-27, which shows structures that lie deep to the ventral surface of the brain. One of the targets of both the central amygdaloid nucleus and the extended amygdala is nucleus basalis, through which it can thus affect neocortical function. These subpallial forebrain components may play a role in the production of appropriate responses—both visceral and somatic—to biologically important events.

Nucleus Basalis of Meynert. The third major part of the ventrolateral forebrain includes a group of large cholinergic neurons that lies within the substantia innominata, some scattered and some in aggregates. These cholinergic neurons are the nucleus basalis of Meynert, or the **magnocellular corticopetal cell complex** (Figs. 19-26 and 19-27). This cell group

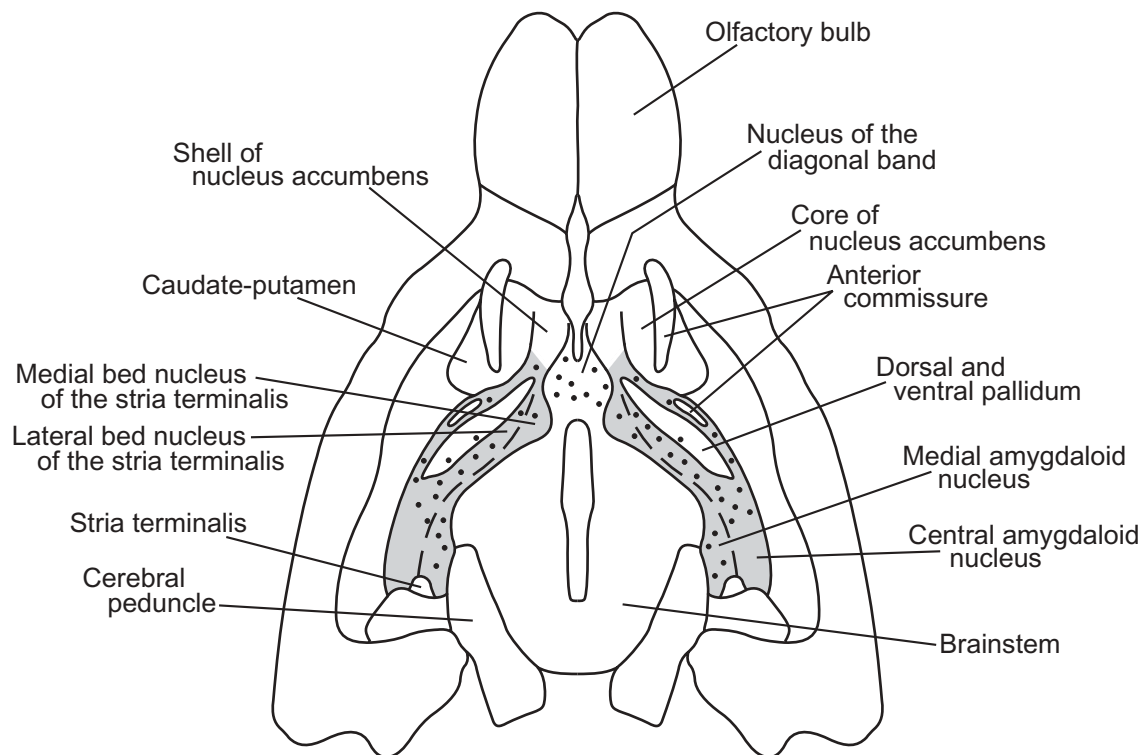


FIGURE 19-27. View of structures deep to the ventral surface of the brain in a rat. Rostral is toward the top. The area of the extended amygdala is indicated by shading, and the distribution of the large cholinergic neurons of nucleus basalis is indicated by the large dots. Adapted from Heimer and Alheid (1991) and used with kind permission of Springer Science and Business Media.

gives rise to a major cholinergic projection to all regions of the neocortex. Three other sets of cholinergic neurons lie within the medial part of the ventral telencephalon (in the medial septal nucleus and in two parts of an L-shaped nucleus ventral to it that is known as the nucleus of the diagonal band of Broca); these will be discussed in Chapters 24 and 30.

The Ventrolateral Telencephalon of Nonmammalian Vertebrates

In reptiles and birds, the striatopallidal areas have been identified on the basis of their connections and histochemical

profiles. Because of recent revisions to the nomenclature for structures in the avian telencephalon, the terminology is now more consistent across amniote taxa than it was previously. The dorsal striatopallidal region is shown in several reptiles in Figure 19-21. The ventral striatopallidal region lies more rostrally than the levels shown in this figure but, as in mammals, consists of a ventral striatum comprised by **nucleus accumbens** and the **olfactory tubercle** and a **ventral pallidum**. Nucleus accumbens and the dorsal striatopallidal cell groups are shown in Figure 19-28 in the forebrain of a turtle; these three sections are at levels rostral to that shown in Figure 19-21A. In turtles, the dorsal striatum has medial and lateral divi-

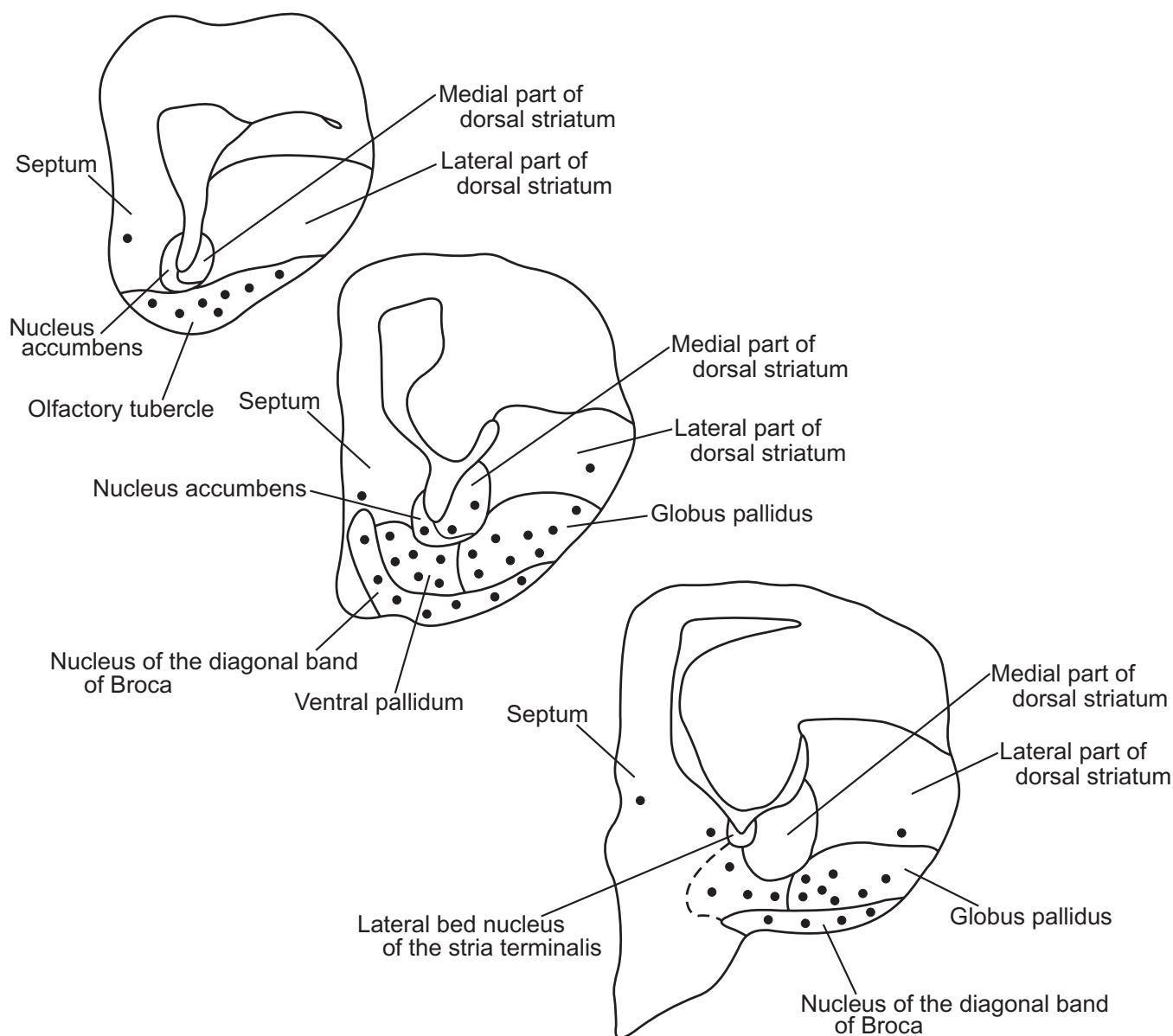


FIGURE 19-28. Drawings of a series of transverse hemisections through the right telencephalon of a turtle, with the most rostral section at the upper left. The distribution of the large cholinergic neurons of nucleus basalis is indicated by the scattered large dots. Adapted from Powers and Reiner (1993) with modifications from Powers and Reiner (1980) and Powers et al. (2003).

sions. The nucleus previously labeled paleostriatum augmentatum is now recognized as the **lateral division of the dorsal striatum**. The **medial division of the dorsal striatum** comprises most of a region that was previously called area d. Nucleus accumbens comprises the ventral-most part of the previously defined area d and all of a more medial region formerly called area c. The **globus pallidus**, which comprises the dorsal pallidum, has been consistently named as such in turtles as in mammals.

Large cholinergic neurons are present in the basal forebrain of reptiles that are homologous to nucleus basalis of mammals. The distribution of these neurons in a turtle is indicated by scattered large dots in Figure 19-28. It is possible that the unlabeled area in the most caudal section shown in Figure 19-28, which is partly bordered by a dashed line medial to the medial part of the dorsal striatum and the globus pallidus, containing scattered large cholinergic neurons, may correspond to the more caudal, sublenticular (i.e., ventral to the lentiform nucleus) part of the substantia innominata and thus to part of the extended amygdala of mammals. Another component of the extended amygdala, the **lateral bed nucleus of the stria terminalis**, is also present at this level. The main nuclei of the amygdala lie more caudally, within the caudal part of the dorsal ventricular ridge, as discussed above.

In birds (Fig. 19-24; Table 19-1), the dorsal striatum comprises two regions named the **lateral striatum** and the **medial striatum**. These regions were previously called the paleostriatum augmentatum and the lobus parolfactorius, respectively. The dorsal pallidum, previously called the paleostriatum primitivum, is now termed the **globus pallidus**, as it is in mammals. In birds, the globus pallidus has only one segment rather than two; nonetheless, the cell populations present in the two segments of mammals are both present within the single dorsal pallidal nucleus of birds. Ventral striatopallidal components are also present in birds. They lie rostral to the level shown in Figure 19-24 and are now given the same names as in mammals—**nucleus accumbens**, **olfactory tubercle**, and **ventral pallidum**. Components of the extended amygdala, including the **lateral and medial bed nuclei of the stria terminalis**, are also now recognized in birds and identified by the same names as in mammals. Likewise, the cholinergic cell population of the ventral telencephalon, previously unnamed and now called **nucleus basalis magnocellularis**, is also present in birds. This new terminology in birds was chosen in order to make it clear that this cell group is the homologue of the magnocellular corticopetal cell complex of mammals.

The Septum

The septum is the second major division of the subpallium. In anamniote vertebrates with evaginated pallia, the septal nuclei lie in the ventromedial wall of the telencephalon, ventral to the medial pallium, as shown in Figures 19-6 and 19-8. They are extensively interconnected with the hypothalamus and the medial pallium. In ray-finned fishes, a medially lying nucleus within the subpallium, called the ventral nucleus of area ventralis (Vv), has similar connections and is a good candidate for a homologue of the septal nuclei of amniotes.

In mammals, the septal area receives the bulk of its afferent input from limbic cortex and the hypothalamus. The rostral

part of the septum contains a lateral and a medial division. The lateral division contains the **lateral septal nuclei** (Fig. 19-26). The medial division contains **medial septal nuclei** and a nucleus called the **nucleus of the diagonal band of Broca** (Fig. 19-26). Cholinergic neurons lie within the latter two regions. Two additional nuclei have been identified in the caudal part of the septum in mammals, called the **septohippocampal nucleus** and the **triangular nucleus**. In reptiles and birds, the septum lies ventral to the medial pallium (Figs. 19-21 and 19-28) and is similarly interconnected with the hypothalamus and the medial pallium. However, the particulars of the connections and histochemical features vary sufficiently to suggest that the septal region may be homologous across amniotes as a field rather than having individual nuclei that are comparable on a one-to-one basis.

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20

Pretectum, Accessory Optic System, and Migrated Posterior Tuberculum

INTRODUCTION

The structures discussed in this chapter lie in the caudal part of the diencephalon, sometimes considered as a transitional region between the diencephalon and the mesencephalon. The pretectum and accessory optic nuclei lie between the dorsal thalamus and the optic tectum. The posterior tuberculum is in the area that is ventral to the pretectum. The degree of development of the components of these sets of nuclei varies markedly across different vertebrate radiations, as do some of their connections.

In this chapter, we will first consider the **pretectum**, a set of nuclei related primarily to the visual system and involved in visuomotor behaviors. Pretectal functions vary across different groups of vertebrates. In ray-finned fishes, some of the pretectal nuclei participate in circuits with the inferior lobe of the hypothalamus, which is involved in feeding behavior. In mammals, the pretectum is involved in several projection systems, including 1) relay of visual information to dorsal thalamic visual nuclei, 2) supplying visual and other sensory information to the vestibulo-ocular system via accessory oculomotor nuclei and other relays to the cerebellum, and 3) regulating pupillary constriction. Birds and reptiles share some of this circuitry with mammals but also have some specialized features.

We will then discuss the **accessory optic nuclei**, which likewise show some variation across vertebrate groups. The accessory optic nuclei are functionally interrelated with the pretectum; in fact, one pretectal nucleus (variously known in amniotes as the nucleus of the optic tract or nucleus lentiformis mesencephali) is best considered as part of the accessory optic

system. Although the accessory optic nuclei actually lie in the tegmentum, their connections and functions can best be understood in relation to the pretectal nuclei. Like the pretectal nuclei, they interact with the vestibulo-ocular system via accessory oculomotor nuclei and inferior olivary projections to the cerebellum, and they also give rise to ascending projections to visual system nuclei in the dorsal thalamus.

In the final part of the chapter, we will discuss the migrated part of the **posterior tuberculum**, which is present only in fishes and is involved in relaying sensory information to the telencephalon. Rather than being associated with the pretectum, the preglomerular nuclear complex is best thought of as a collection of dorsal thalamus-like, diencephalic relay stations. It is discussed here because of its location in the caudal part of the diencephalon.

PRETECTUM

The pretectal nuclei receive afferents primarily from the retina and the optic tectum and are involved in modulating motor behavior in response to visual input. In some Group I vertebrates as well as in Group II vertebrates, lateral migration of pretectal neurons occurs during development. In these animals, three pretectal zones, or sets of nuclei, can be identified: **superficial**, **central**, and **periventricular**. The periventricular zone curves around a caudally running fiber tract that originates in the habenula and is called the **fasciculus retroflexus**. This tract serves as a convenient landmark in the pretectal region but does not carry pretectal fibers.

Group I

In lampreys, the pretectum lies caudal to the dorsal thalamus and can be divided dorsoventrally into three tiers (Fig. 20-1). In all three of these tiers, the majority of neuron cell bodies lies near the ventricular surface. The pretectum receives an input from the retina. Although most of its other connections have not been studied, it is known to project bilaterally to the reticular formation. This pretectoreticular pathway is crucial for two reflexive responses that lampreys make to illumination of an eye—the dorsal light reflex (see Chapter 14), which involves a roll to tilt the body toward the light, and subsequently negative phototaxis, which consists of swimming away from the light. Lesion experiments have shown that the contralateral pretectoreticular pathway mediates the former, while the ipsilateral pathway mediates the latter.

In squalomorph sharks (Fig. 20-2), some migration of neurons occurs during the development of the pretectum. A **superficial pretectal nucleus** lies in a lateral position, and a **central pretectal nucleus** is present lateral to the posterior commissure. These two nuclei receive retinal projections. A cell group medial to the central pretectal nucleus constitutes a **periventricular pretectal nucleus**. The optic tectum projects to all three pretectal nuclei.

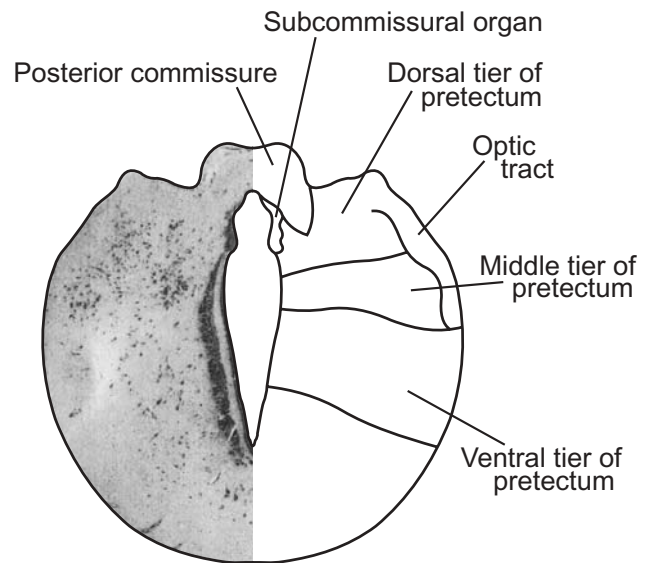


FIGURE 20-1. Transverse hemisection with mirror-image drawing through the pretectum of a lamprey (*Lampetra fluviatilis*). Adapted from Pombal and Puelles (1999) and used with permission of John Wiley & Sons.

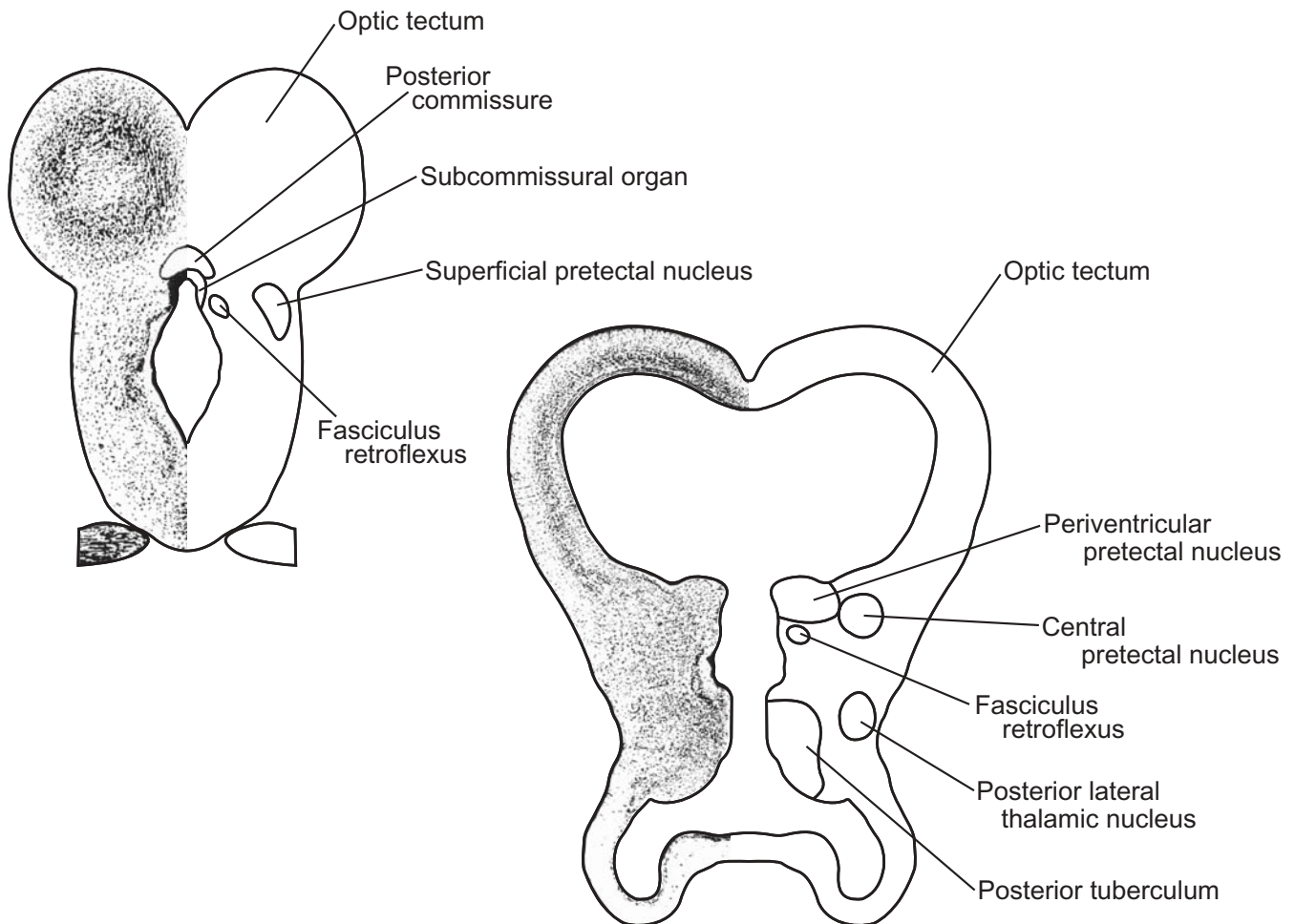


FIGURE 20-2. Transverse hemisections with mirror-image drawings through the pretectum of a shark (*Squalus acanthias*). The more rostral section is at the upper left. Adapted from Northcutt (1978) with additional data from Smeets and Northcutt (1987).

In the pretectum of nonteleost ray-finned fishes, some neuronal migration also occurs during development. Pretectal nuclei are present in the superficial, central, and periventricular zones, that is, superficial to deep regions that are in continuity with similarly named zones of the optic tectum (see Chapter 18). In reedfishes and sturgeons, one pretectal nucleus is present in the superficial zone and is characterized by small cells: the **parvocellular superficial pretectal nucleus**. In gars and the bowfin *Amia* and also in teleosts, as we will discuss below, several superficial nuclei are present (Fig. 20-3). It is possible that one or two of these nuclei (particularly nucleus corticalis) more properly belong in the central zone, but we will consider them all here due to their functional relationships and connections.

In gars and in *Amia*, the **parvocellular superficial pretectal nucleus**, a nucleus with large, widely scattered cells called the **magnocellular superficial pretectal nucleus**, and a more medially lying nucleus called the **posterior pretectal nucleus** are present in the superficial zone. In *Amia*, and possibly in gars, an additional nucleus, called **nucleus corticalis**, is present in this region. The parvocellular superficial pretectal nucleus and nucleus corticalis receive retinal projections, and the magnocellular superficial pretectal nucleus receives tectal projections. Additional connections of these nuclei have been studied in teleosts, and they have been reported to be involved in linking visual input to motor behaviors related to feeding.

A **central pretectal nucleus** lies in the central pretectal zone of nonteleost ray-finned fishes. **Dorsal** and **ventral periventricular pretectal nuclei** occupy the periventricular pretectal zone. The retina projects to the central pretectal nucleus and to the ventral and dorsal periventricular pretectal nuclei. The optic tectum projects to the central pretectal nucleus and the dorsal periventricular pretectal nucleus.

Among amphibians, the pretectum is somewhat more differentiated in anurans than in urodeles. In anurans (Fig. 20-4), at least five pretectal nuclei are present: the **posterior thalamic nucleus**, the **posterodorsal division of the lateral thalamic nucleus**, **nucleus lentiformis mesencephali**, the **nucleus of the posterior commissure**, and the **pretectal gray**. The first two of these nuclei have sometimes been grouped as a posterior part of the dorsal thalamus, but since they do not project to any part of the telencephalon, they are included in the pretectum here.

A number of the connections of the various pretectal nuclei have been described in frogs. Nucleus lentiformis mesencephali contains large cells and receives the heaviest retinal input. As discussed below for amniotes, this nucleus is considered in the section on the accessory optic system, since it is best understood as a component of that system. The additional inputs that nucleus lentiformis mesencephali receives need to be mentioned here, however, since the dendrites of neurons in the posterior thalamic nucleus extend into nucleus lentiformis mesencephali and thus also may receive these inputs, which include projections from the optic tectum, dorsal thalamus, and accessory optic nucleus. The posterior thalamic nucleus also receives direct input from the retina, optic tectum, and dorsal thalamus, as well as additional inputs from the striatopallidum, ventral hypothalamus, and a variety of other sources. It projects to more rostral thalamic nuclei, including nucleus anterior, and to the optic tectum and torus

semicircularis. Additionally, the posterior thalamic nucleus gives rise to descending brainstem projections, including a projection to the abducens nucleus. The posterodorsal division of the lateral thalamic nucleus, which also receives pallidal input, projects to the optic tectum and brainstem. The pretectal gray relays hypothalamic input to the brainstem.

A pretectal nucleus that mediates the pupillary light reflex, which is constriction of the pupil in response to light, has not been identified in frogs. They have a small ciliary ganglion, and a few cells have been identified that lie dorsal to the main oculomotor nuclear complex, which may constitute an Edinger-Westphal nucleus. Pretectal pathways to these cells remain to be investigated, however.

Efferent projections of the pretectum also have been studied recently in urodeles. In a salamander, the **nucleus praetectalis profundus**, which lies lateral to the posterior commissure, gives rise to widespread projections. Within the forebrain, it projects to both the amygdala and the striatum, as well as to the dorsal thalamus and to the contralateral pretectum. It also projects to the optic tectum and rather diffusely to the tegmentum. Descending projections extend to the medulla oblongata and to the rostral part of the spinal cord. These projections thus probably include connections with the vestibulo-ocular system as in other vertebrates.

Also in urodeles, the neural basis for pupillary constriction in response to increased illumination has been identified. A **nucleus praetectalis olivaris**, of the same name as its homologue in mammals, is located in the same general region as the nucleus praetectalis profundus, but the neurons tend to lie slightly more ventrally and caudally. This nucleus has been found to project bilaterally to the parasympathetic division (Edinger-Westphal) of the oculomotor nucleus, which in turn innervates the ciliary ganglion and mediates constriction of the pupil. The bilaterality of the projection is noteworthy because the homologous pathway is also bilateral in mammals but is only contralateral in birds, as discussed below.

The pretectum in both frogs and salamanders is involved in regulating responses to prey objects. Under normal circumstances, the pretectum inhibits prey-catching responses to objects that are too large to fall within the range of suitable prey items. This inhibition is mediated via the pretectal projections to the optic tectum. Lesions of the pretectum result in disinhibition such that the animals attempt to feed not only on normal prey-sized objects but also on larger and thus potentially threatening objects. They also fail to make appropriate avoidance responses to the latter.

Group II

Anamniotes. In hagfishes, relatively limited migration of pretectal neurons occurs during development. Two nuclei (Fig. 20-5) have been identified in the pretectum and lie in the central to periventricular region: the **pretectal nucleus**, which lies lateral to the posterior commissure, and the **nucleus of the posterior commissure**, which lies ventral to the pretectal nucleus. The pretectal nucleus receives a substantial retinal projection.

In Group II cartilaginous fishes, the pretectum has superficial, central, and periventricular zones (Fig. 20-6). All three zones receive both retinal and tectal projections. The superfi-

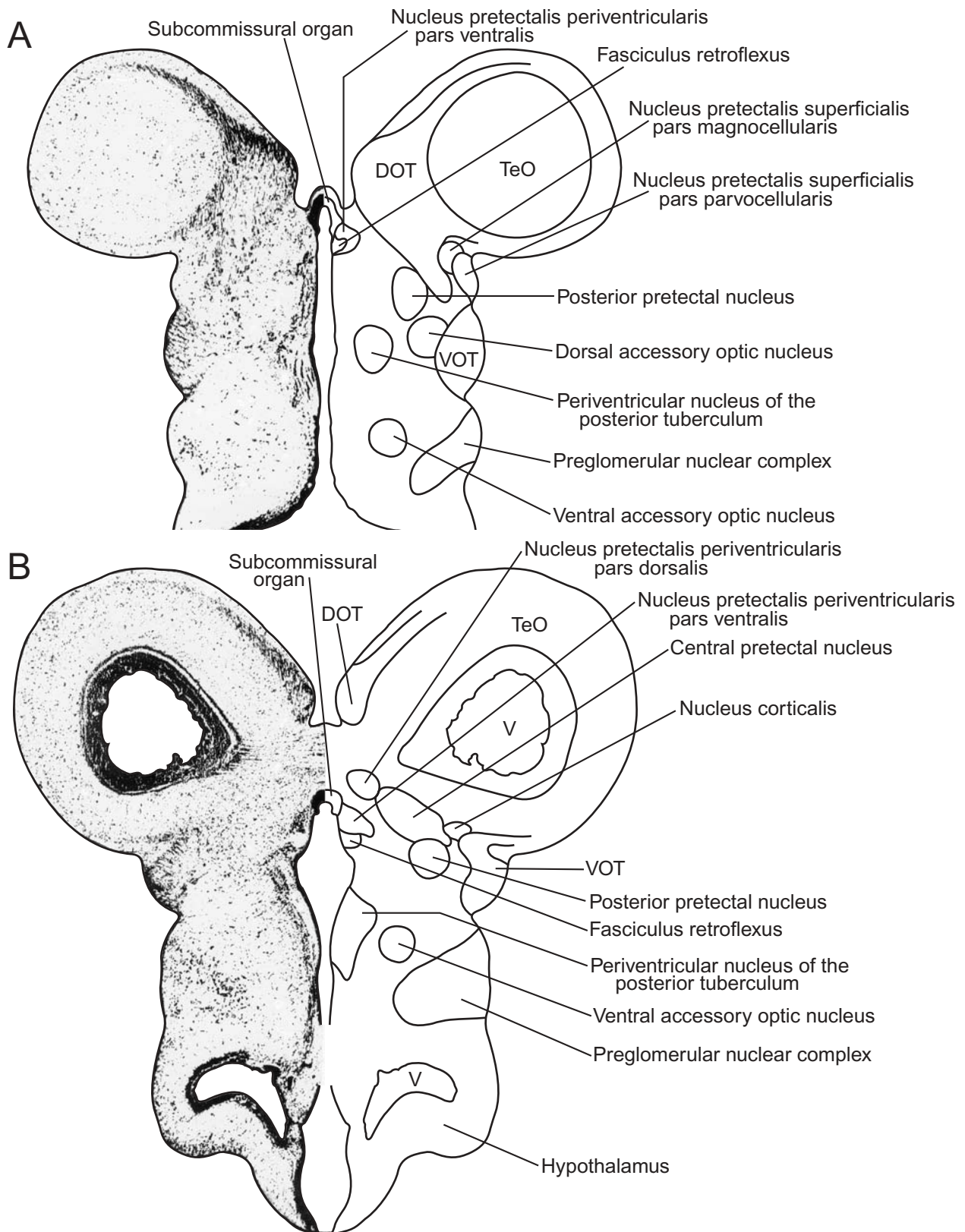


FIGURE 20-3. Transverse hemisections with mirror-image drawings through the prepectum of a bowfin (*Amia calva*), with A being more rostral. Adapted from Butler and Northcutt (1992). Abbreviations: DOT, dorsal optic tract; TeO, optic tectum; V, ventricle; VOT, ventral optic tract. Used with permission of S Karger AG, Basel.

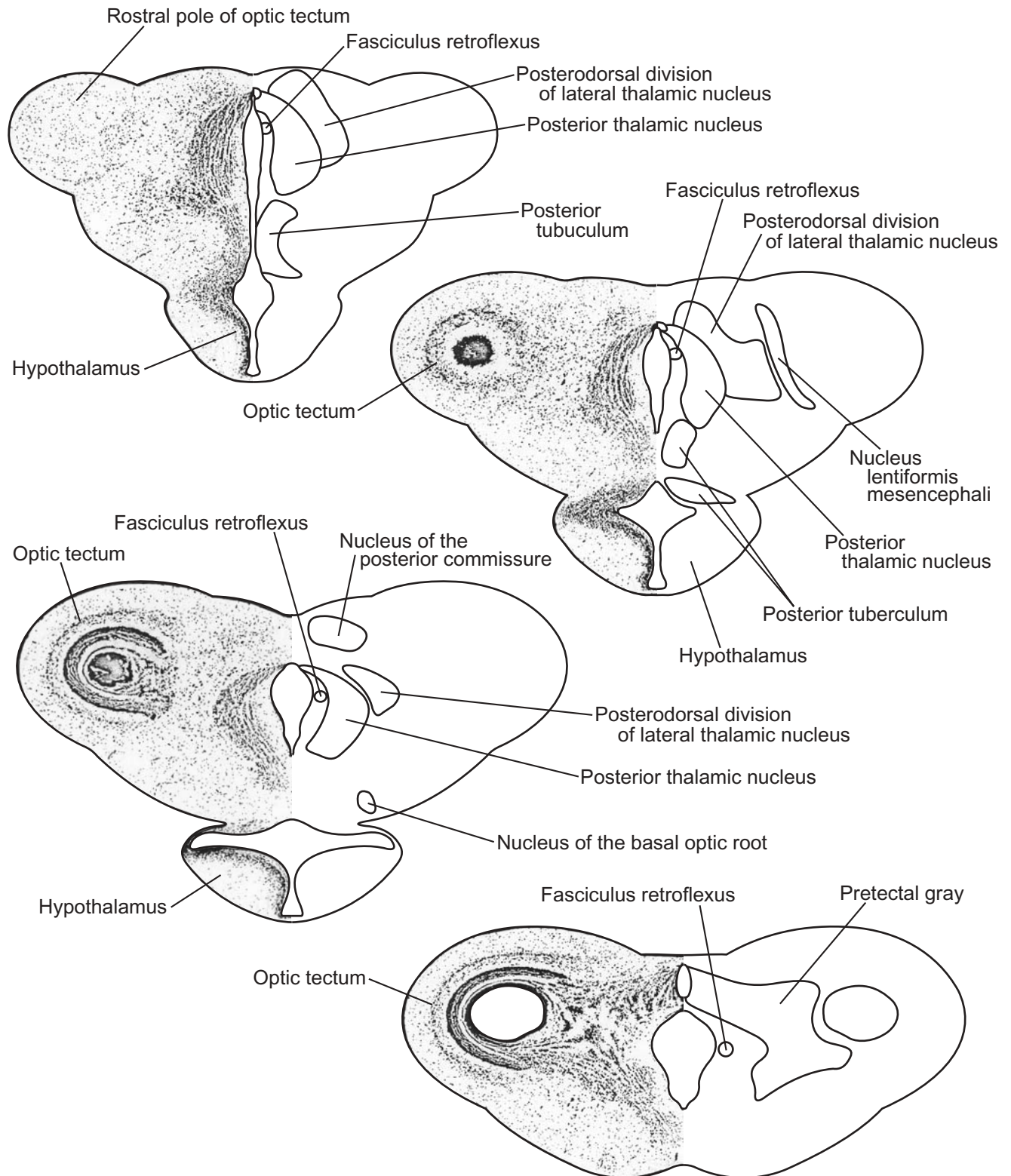


FIGURE 20-4. Transverse hemisections with mirror-image drawings through the pretecrum of a frog (*Rana catesbeiana*). The most rostral section is at the top left and the most caudal at the bottom right. Adapted from Neary and Northcutt (1983) and used with permission of John Wiley & Sons.

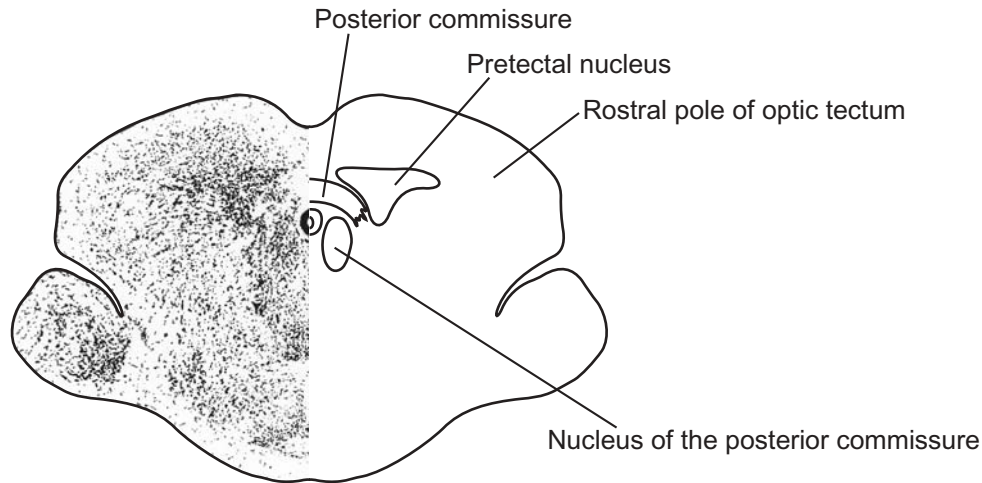


FIGURE 20-5. Transverse hemisection with mirror-image drawing through the pretectum of a hagfish (*Eptatretus stouti*). Adapted from Wicht and Northcutt (1992) and used with permission of S Karger AG, Basel.

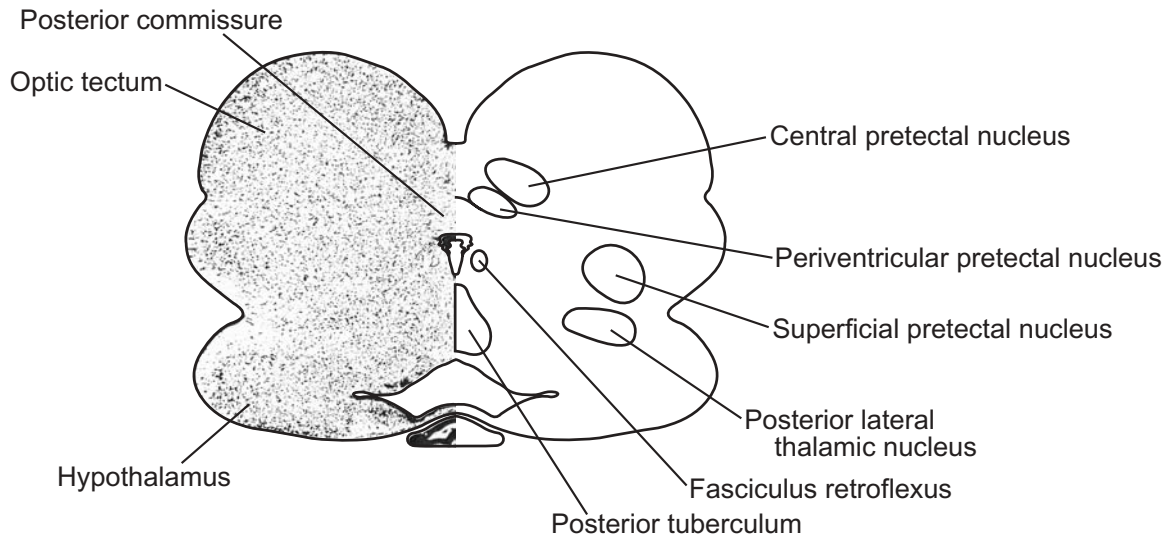


FIGURE 20-6. Transverse hemisection with mirror-image drawing through the pretectum of a skate (*Raja eglanteria*). Adapted from Northcutt (1978) with additional data from Bodznick and Northcutt (1984).

cial pretectal zone (or nucleus) projects to the cerebellum. No part of the pretectum gives rise to telencephalic projections, but most of the efferent projections of the pretectum to nuclei in the brainstem remain to be studied.

In teleosts (Fig. 20-7), the pretectal nuclei are more numerous and distinct than in other ray-finned fishes or in cartilaginous fishes. In fact, a marked hypertrophy of the pretectal and posterior tubercular regions is one of the hallmarks of teleosts, in direct contrast to the hypertrophy of the dorsal thalamus in amniotes, which we will consider in Chapter 22. The pretectal components vary across different taxa of teleosts, so we will note some of the variations in the context of a general overview.

The periventricular pretectal zone contains two nuclei: a **ventral periventricular pretectal nucleus (PPv)** and a **dorsal periventricular pretectal nucleus (PPd)**. (The dorsal periventricular pretectal nucleus sometimes is called the **optic nucleus of the posterior commissure**.) In some teleosts, including ostariophysans and percomorphs, a third periventricular pretectal nucleus is present: the **paracommissural nucleus**. When present, it lies dorsal to the dorsal periventricular pretectal nucleus. The central pretectal zone is an area of scattered cells called the **central pretectal nucleus (PC)**. The borders of this nucleus are often difficult to distinguish. Both the central and periventricular pretectal zones of teleosts are similar to those in other fishes.

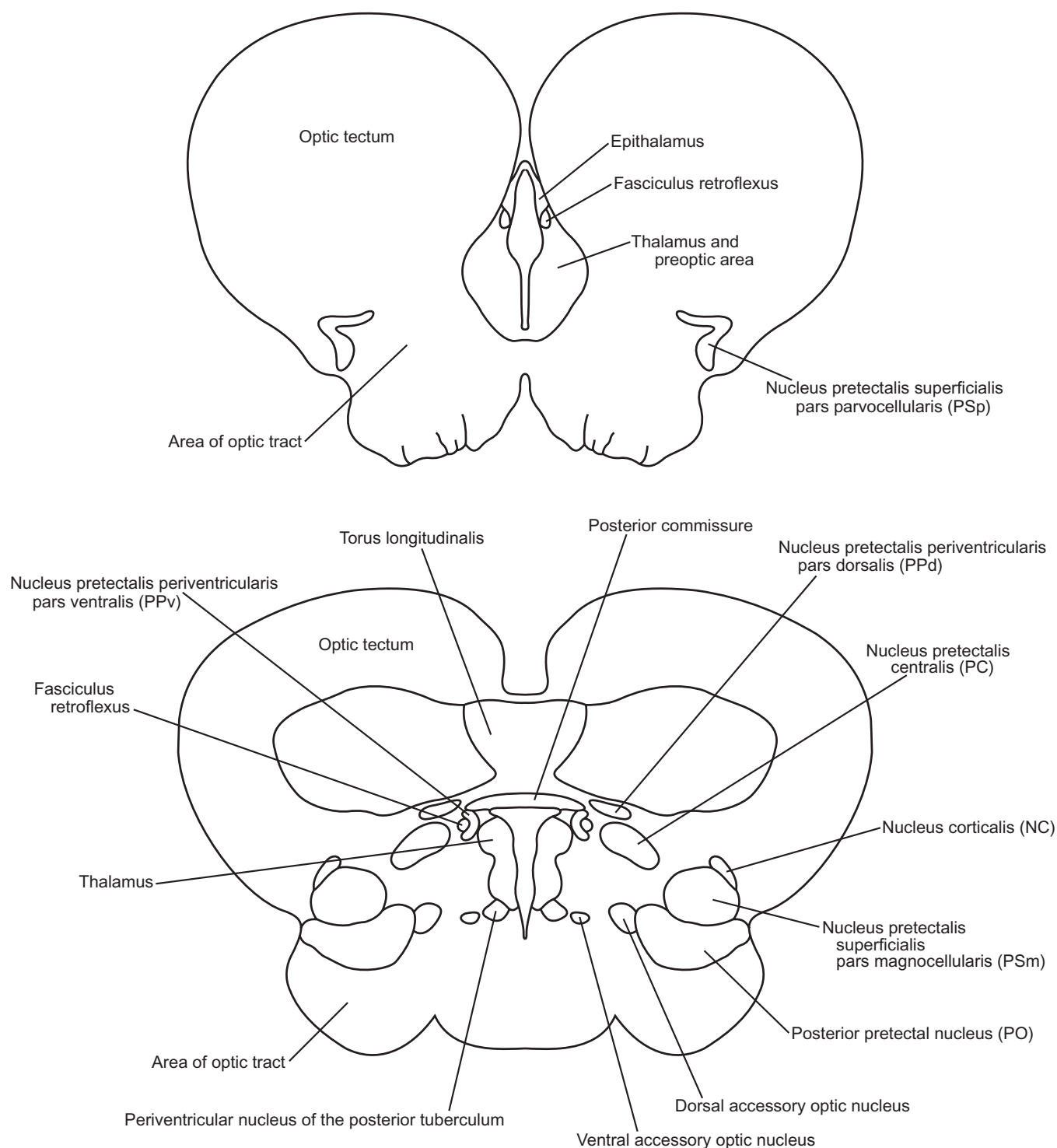


FIGURE 20-7. Drawings of transverse sections through the pretectum of a teleost (*Clupea harengus*). The more rostral section is at the top. Adapted from Butler and Northcutt (1993).

The superficial preectal zone is markedly expanded in most teleosts and contains a number of nuclei. The most rostral of these nuclei is the **parvocellular superficial preectal nucleus (PSP)**. This nucleus lies at a point of bifurcation of the optic tract into dorsal and ventral optic tracts. It receives a sub-

stantial retinal projection and a tectal projection as well. It also receives an input from nucleus isthmi. The parvocellular superficial preectal nucleus has been identified incorrectly in earlier literature as the retino-recipient nucleus of the dorsal thalamus and hence called the dorsal lateral geniculate nucleus.

The superficial zone of the pretectum in teleosts also contains a **magnocellular superficial pretectal nucleus (PSm)**, which receives a tectal projection, and a **nucleus corticalis (NC)**, which receives retinal and, probably, tectal projections. In three of the four groups of teleost fishes, one additional nucleus, the **posterior pretectal nucleus (PO)**, is also present. In the fourth and largest group of teleosts, the euteleosts, two additional nuclei are present, which are homologous as a field to the posterior pretectal nucleus of the other ray-finned fishes. These nuclei are called the **intermediate superficial pretectal nucleus (PSi)** and **nucleus glomerulosus (G)**.

Visual information is relayed through some of these superficial pretectal nuclei to part of the hypothalamus, and this pathway is thought to be involved in orienting the fish's body to the location of a food object. In most groups of ray-finned fishes, this pathway is from the parvocellular superficial pretectal nucleus and nucleus corticalis to the posterior pretectal nucleus, and thence to the **inferior lobe of the hypothalamus (LI)** [Fig. 20-8(A)]. In euteleosts [Fig. 20-8(B)], the parvocellular superficial pretectal nucleus and nucleus corticalis project to the intermediate superficial pretectal nucleus (PSi), which, in turn projects to nucleus glomerulosus. The latter projects to the inferior lobe of the hypothalamus. The parvocellular superficial pretectal nucleus also has more direct projections to motor system structures, including the trochlear nucleus (**IV**) and the inferior raphe (**IR**), the latter projecting, in turn, to the spinal cord.

Marked variation occurs in the size and shape of some of the pretectal nuclei across different taxa of teleosts, and some examples of this variation are shown in Figure 20-9. The parvocellular superficial pretectal nucleus, PSp, of the salmon (A), a euteleost, has a bi-laminar configuration. In contrast, in one osteoglossomorph teleost, the freshwater butterfly fish *Pantodon* (C), it has a simple oval shape, while in another osteoglossomorph, the arawana *Osteoglossum* (D), it has an elongated profile and is shaped like the letter U. Nucleus corticalis also varies substantially in its configuration. In some euteleosts, particularly the salmon *Salmo* (A, B) and the trout *Esox* (H, I), the cells of this nucleus are not aggregated into a discrete region but instead are scattered within the ventrolateral aspect of the optic tectum. In contrast, in most teleosts, nucleus corticalis is a discrete group of neurons, such as in the osteoglossomorph *Osteoglossum* (F) and the euteleost sunfish *Lepomis* (K, L).

The posterior pretectal nucleus, where present, also varies greatly in its size among different species. In gars and in *Amia*, as discussed above, it is small. Among teleosts, the size of the nucleus varies from very small to extremely large. As shown in Figure 20-9, for example, the posterior pretectal nucleus is very large in *Osteoglossum* (E-G) but moderate to small size in the two teleosts *Salmo* (A, B) and *Esox* (H-J). In euteleosts, such as the sunfish *Lepomis* (K-P), two nuclei have differentiated in place of the single posterior pretectal nucleus, and the morphology of one of these nuclei, nucleus glomerulosus, is particularly complex, with concentric layers of cells and fibers. The different feeding behaviors in various groups of ray-finned fishes are possible due to these marked differences in the nuclear structure of the pretectal region.

Another nucleus, the magnocellular superficial pretectal nucleus (PSm), may have different connections in two groups of euteleosts or, in one group or the other, may have been lost and replaced by a different cell population. This nucleus receives input from the optic tectum. In sunfishes (*Lepomis cyanellus*) and filefishes (*Navodon modestus*), which are percomorph euteleosts [Fig. 20-8(C)], it projects to two nuclei that, in turn, project back to the optic tectum. One of these nuclei is nucleus isthmi (see Chapter 16), which also projects to the corpus cerebelli. The second nucleus is called the lateral thalamic nucleus; it is discussed below with the migrated nuclei of the posterior tuberculum. In goldfishes (*Carassius auratus*), which are ostariophysan euteleosts [Fig. 20-8(D)], PSm projects to two different nuclei—a cerebellar nucleus called nucleus lateralis valvulae, which projects to the cerebellum and also is reciprocally connected with the inferior lobe (LI) of the hypothalamus, and another nucleus called the mammillary body, which is part of the posterior tuberculum. In both percomorphs and goldfishes, projections from PSm are relayed to the cerebellum, albeit by different routes. The pathways through PSm may modulate the visuomotor orienting behavior that is achieved with the pathways through PSp. A nucleus homologous to PSm is also present in tilapia (*Oreochromis niloticus*), another percomorph euteleost, but in this fish it has been identified as the pars anterior of the corpus glomerulosum. This nucleus projects to the lateral valvular nucleus as does PSm in ostariophysans.

More studies are needed to determine which set of projections of PSm are present in most euteleosts and what the changes have been in one group or the other. Whatever the outcome, this part of the pretectum exhibits the potential for marked variation of central nervous system structure among species, whether in the cell populations present and/or in changes of their connections.

An additional pretectal nucleus is present in at least some percomorph euteleosts but absent in ostariophysans. This nucleus is simply called nucleus pretectalis. It projects to nucleus isthmi, which in turn has extensive and reciprocal connections with the optic tectum (see Chapter 16). Nucleus isthmi also projects to the parvocellular superficial pretectal nucleus. No nucleus that projects to nucleus isthmi has been found within the pretectum in ostariophysans—carp being the particular taxon examined.

Mammals. In monotremes, the pretectum is not a well-differentiated area, in contrast to the pretectum in other mammals and in reptiles and birds. Only a small pretectal nucleus is present in monotremes, and it is called the **area pretectalis**.

In placental mammals, terminology for the pretectal nuclei varies, particularly between primate and nonprimate species. Five pretectal nuclei generally can be recognized: the **nucleus of the optic tract**, the **olivary pretectal nucleus**, and the **anterior**, **posterior**, and **medial pretectal nuclei**. These nuclei are shown in drawings of the cat brainstem in Figure 20-10 with some of the other nuclei in the same region shown for orientation. The nucleus of the optic tract, or **NOT**, is better considered as part of the accessory optic system and thus will be discussed below in that section.

The two most prominent sources of input to the pretectum are the retina and a number of the visual cortical areas.

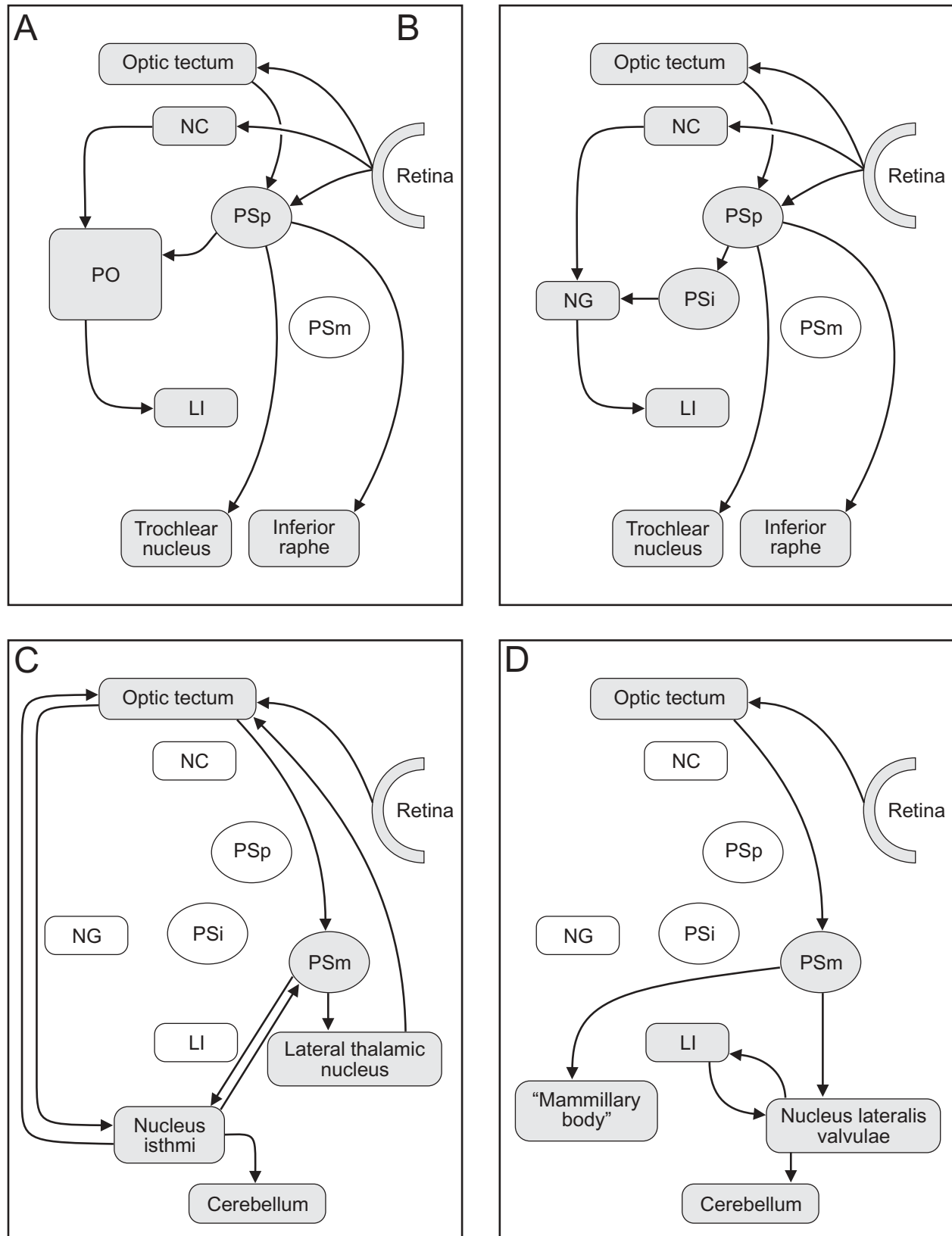


FIGURE 20-8. Diagram of pretectal pathways by which visual information reaches the inferior lobe of the hypothalamus in most groups of ray-finned fishes (A) and euteleosts (B). Diagram of the differing connections of nucleus preectalis superficialis pars magnocellularis in percomorph euteleosts (C) and ostariophysan euteleosts (D). Abbreviations are given in the text.

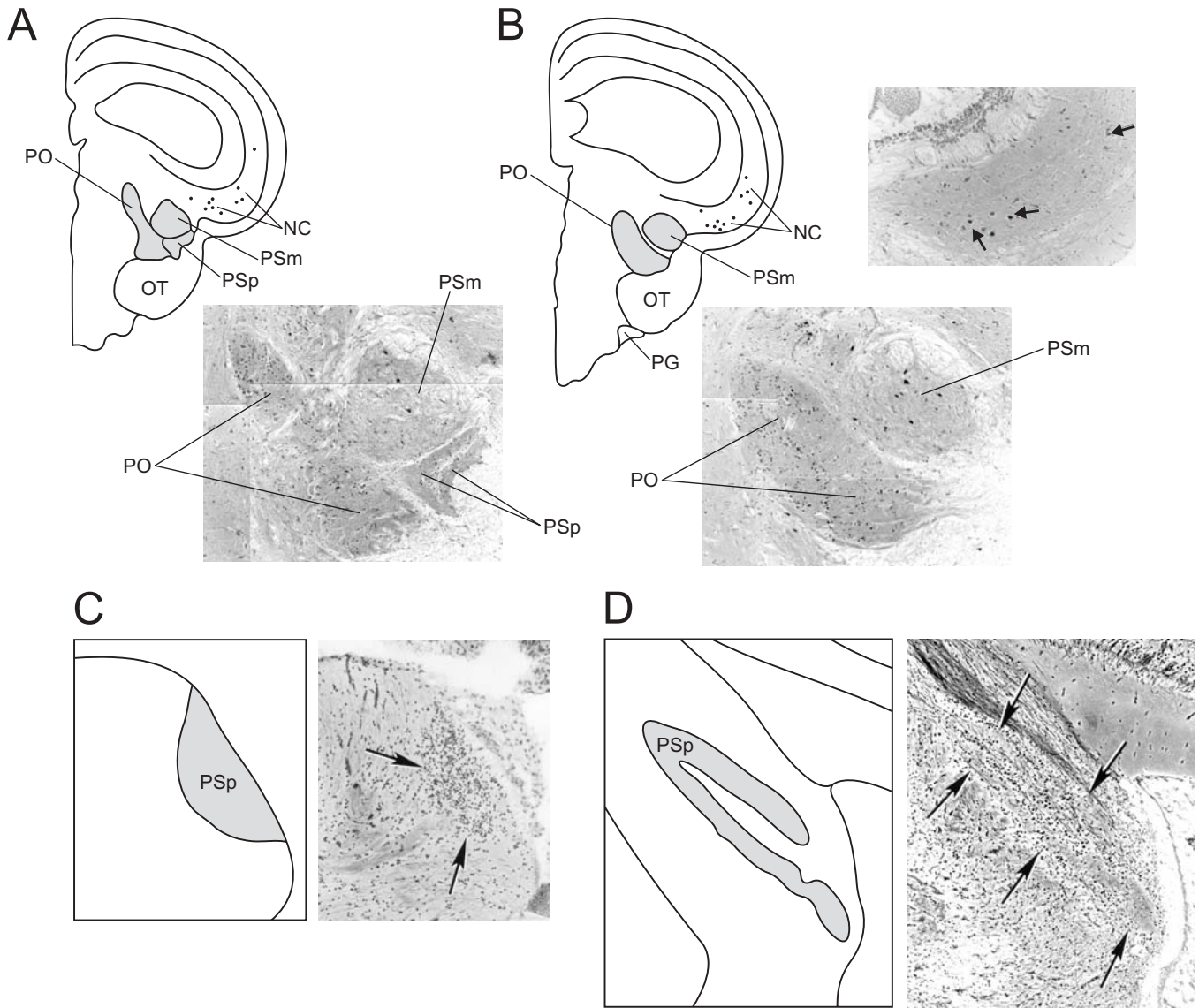
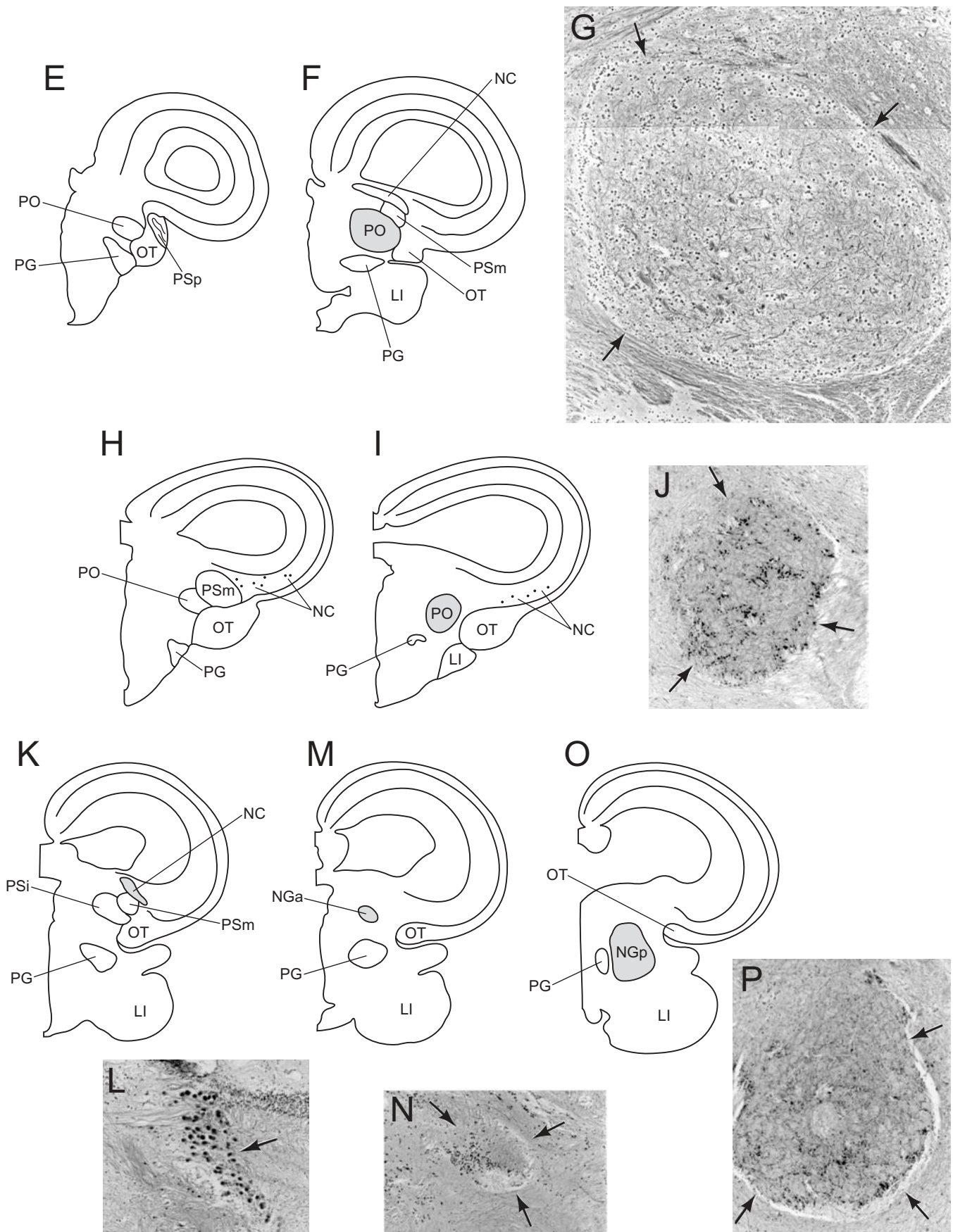


FIGURE 20-9. Drawings of hemisections through the pretectal region on the right side in a euteleost, the salmon *Salmo* (A and B) with photomicrographs to the lower right of each drawing, showing pretectal nuclei as labeled and as indicated by shading in the drawings. The photomicrograph to the right of the drawing in B shows nucleus corticalis (NC) cells (arrows) scattered in the ventrolateral quadrant of the optic tectum. The photomicrographs and drawings in C and D show variation in the shape of PSp in two osteoglossomorph teleosts: in the freshwater butterfly fish *Pantodon* (C) PSp is a simply-shaped, somewhat oval nucleus, whereas in the arawana *Osteoglossum* (D), PSp has an elongated U-shape. Drawings of hemisections (E and F) through the pretectal region on the right side in the arawana *Osteoglossum* and a photomicrograph (G) of the very large posterior pretectal nucleus in this species. For comparison, similar drawings and a photomicrograph of the relatively small posterior pretectal nucleus are shown for the trout *Exox* (H–J). Note that in *Exox*, as for the closely related *Salmo* (A and B), nucleus corticalis cells are scattered in the ventrolateral part of the tectum. Rather than having a single posterior pretectal nucleus, the sunfish *Lepomis*, a euteleost, has two nuclei, PSi (indicated in K) and nucleus glomerulosus, which has a small anterior part, NGa (M and N) and a larger, more ventrally situated part, NGp (O and P). Note that in *Lepomis*, nucleus corticalis is a discrete nucleus (L). Abbreviations: OT, optic tract; the remainder are given in the text. A, B, and E–P adapted from Butler et al. (1991); C and D adapted from Saidel and Butler (1991); all used with permission of S Karger AG, Basel.

**FIGURE 20-9.** (Continued)

The retina projects to the olivary pretectal nucleus and to the posterior pretectal nucleus in most placental mammals. It may also project to either the medial or the anterior pretectal nucleus, depending on the species. There is some indication of topographical order in the retinal projections to the pretectum. Several pretectal nuclei receive projections from primary and association areas of visual cortex. Striate and various extrastriate (visual) cortical areas project to the olivary pretectal nucleus and to the anterior and posterior pretectal nuclei. The pretectum also receives inputs from other sources, including additional visual inputs from the superior colliculus and, particularly to the posterior pretectal nucleus, somatosensory inputs from the dorsal column nuclei and spinal cord.

The pretectum in mammals is involved in the relay of visual input to both ascending systems and to those involved in visuomotor responses. The olivary pretectal nucleus and the anterior and posterior pretectal nuclei project to the dorsal thalamus (see Chapter 22), specifically to the lateral posterior-pulvinar complex, which is a major target of the superior colliculus. Additionally, the posterior pretectal nucleus projects to the dorsal lateral geniculate nucleus, which in turn projects to primary visual cortex.

The anterior, posterior, and medial pretectal nuclei also give rise to descending projections that reach the vestibular nuclei by various routes (Fig. 20-11) and thus contribute to the vestibulo-ocular system. They project to a variety of targets, including the inferior olivary nucleus, dorsolateral pontine nucleus, and reticular formation, which relay these inputs to the cerebellar cortex. Additionally, these pretectal nuclei project to accessory oculomotor nuclei that lie around the main oculomotor complex, particularly the **nucleus of Darkschewitsch** and the **interstitial nucleus of Cajal** (Fig. 20-10). The latter nuclei affect the somatic efferent, neuronal cell groups of the main oculomotor nuclear complex by both direct and indirect routes. The interstitial nucleus of Cajal projects directly to the oculomotor complex, but it and the nucleus of Darkschewitsch, as well as another accessory oculomotor nucleus called the **nucleus of Bechterew**, also project to the inferior olivary nucleus, which in turn projects to the cerebellar cortex.

The cerebellum influences the vestibular nuclei both via direct, reciprocal projections and through the projection of its fastigial nucleus. The vestibular nuclei also have direct, reciprocal connections with the interstitial nucleus of Cajal, and they additionally project to the nucleus of Darkschewitsch (Fig. 20-11). The vestibular nuclei receive input from the vestibular system receptors in the inner ear, and they are thus in a position to integrate this vestibular input with the multiple visual inputs from the pretectal nuclei. They then provide a substantial input to the somatic efferent oculomotor complex. Thus, the vestibulo-ocular system, which is strongly affected by the inputs from the vestibular receptors, is modulated by pretectal visual inputs relayed through multiple routes, including 1) directly from the interstitial nucleus of Cajal to the vestibular nuclei as well as 2) multisynaptically through the inferior olivary nucleus (directly plus via the accessory oculomotor nuclei), dorsolateral pons, and reticular formation to the cerebellum and thence to the vestibular nuclei. As discussed

below, the accessory optic system provides inputs to the vestibulo-ocular system that are similar to those via the pretectal nuclei.

The posterior pretectal nucleus and an adjoining region may also be involved in the relay of basal ganglia inputs to the superior colliculus. In rats, the globus pallidus has been found to give rise to a minor projection to this part of the pretectum, which in turn projects to the superior colliculus. In contrast to the situation mammals, as discussed below, pallidopretectal projections are robustly present in both reptiles and birds and in fact form an important part of a basal ganglia-pretecto-tectal circuit for motor influences on the output of the tectum.

Rather than contributing to the control of eye movements, the olivary pretectal nucleus is involved in pupillary constriction. This nucleus gives rise to LP/pulvinar projections as mentioned above, but its major output is to the general visceral efferent neurons of the Edinger-Westphal nucleus, and it is a crucial component of the circuitry for pupillary constriction in response to illumination of the pupil. In mammals, constriction of the pupil is mediated by a doubly redundant system. The retinal input to the olivary pretectal nucleus is bilateral, and the olivary pretectal nucleus in turn projects bilaterally to the Edinger-Westphal nucleus, with its contralaterally running fibers decussating in the posterior commissure. The parasympathetic neurons of the Edinger-Westphal nucleus then ipsilaterally innervate the ciliary ganglion, which in turn innervates the pupillary constrictor muscle of the pupil. Thus, shining a light into either eye results in constriction of both pupils, and unequal pupil size is regarded as a sign of pathology of this system.

Reptiles and Birds. Among amniotes, the pretectum is relatively larger in nonmammalian amniotes than in mammals. In various squamate reptiles and turtles, 5–10 pretectal nuclei have been recognized, depending on the taxon (Fig. 20-12). In lizards, three pretectal nuclei that receive retinal input are **nucleus geniculatus pretectalis**, **nucleus lentiformis mesencephali**, and **nucleus posterodorsalis**. Nuclei lentiformis mesencephali and geniculatus pretectalis also receive input from the optic tectum, which receives reciprocal input from the former as well as an input from nucleus posterodorsalis. The telencephalon projects to an additional, more medially lying pretectal nucleus called the nucleus of the posterior commissure (not shown in Fig. 20-12), which relays this input to the cerebellum. (A nucleus of the posterior commissure is also present in mammals, as shown in Fig. 20-10 and discussed below, but it is usually classified as an accessory oculomotor nucleus rather than as a component of the pretectum per se.) Additional pretectal nuclei in lizards lie more caudally and can be grouped as subdivisions of one larger area termed **nucleus lentiformis thalami**. The subdivisions include a **pars plicata** (meaning “folded” in Latin), a **pars extensa** (meaning “stretched out”), the **dorsal pretectal nucleus**, and the **medial pretectal nucleus**. The pars plicata and pars extensa of nucleus lentiformis thalami lie in the periventricular zone of the pretectum, while the dorsal and medial pretectal nuclei occupy the central zone. A **ventral pretectal nucleus** has also been recognized in some species.

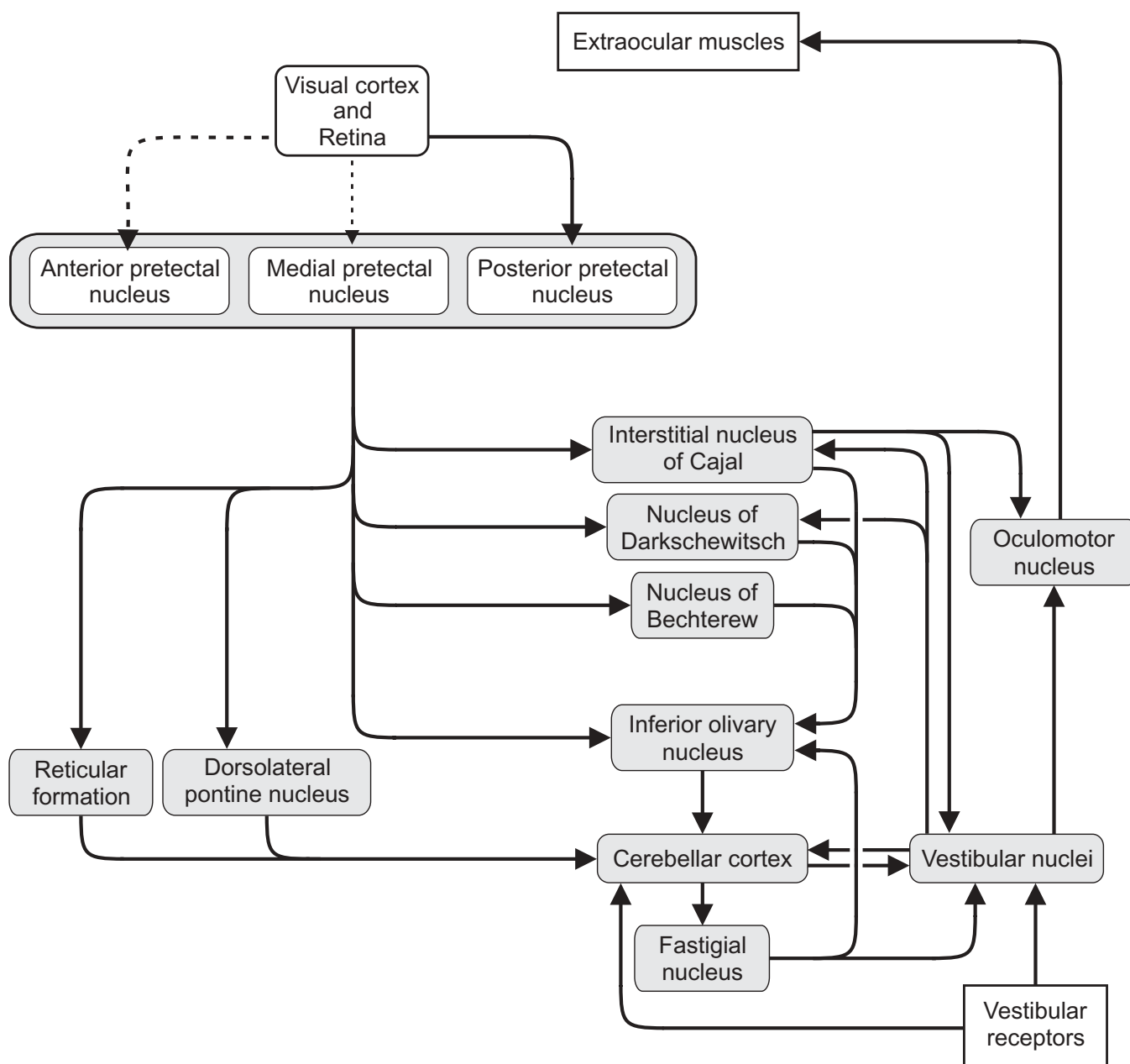


FIGURE 20-11. Diagram of the multiple routes in mammals from the anterior, medial, and posterior pretectal nuclei to the vestibular nuclei, which in turn influence the oculomotor nucleus and the position of the eyes. Dashed lines indicate uncertainty as to projection and/or variability among species.

Where present, this nucleus lies in the superficial part of the pretectum.

A number of pretectal nuclei have been identified in turtles, some of which are clearly homologous to nuclei of the same name in lizards and others of which remain to be comparatively classified. As in lizards, nuclei geniculatus pretectalis, lentiformis mesencephali, and posterodorsalis are present. A nucleus not yet identified in lizards, the **griseus tectalis**, or **tectal gray**, lies dorsal to nucleus lentiformis mesencephali along the base of the optic tectum. These four nuclei all receive

retinal projections, as does an additional nucleus called the **posterior nucleus**. The posterior nucleus receives an afferent input from the globus pallidus; it and another pretectal cell group called the **dorsal nucleus of the posterior commissure** both project to the optic tectum. These two tectopetally projecting pretectal nuclei appear to be homologous to the lateral spiriform nucleus (discussed below) of birds, which also relays pallidal inputs to the tectum. These nuclei in sauropsids may be homologous to the posterior pretectal nucleus of mammals, but while the pallidal relay to the optic tectum is a

shared feature, other connections and the topographical positions of these nuclei argue against this comparison. Additional pretectal cell groups recognized in turtles include nuclei **pretectalis dorsalis**, **pretectalis ventralis**, **opticus pretectalis ventrolateralis** (which is retinorecipient), and an **interstitial nucleus of the posterior commissure**, which has dorsal and ventral divisions.

The pretectum has been less extensively analyzed in crocodiles than in lizards and turtles, but some corresponding cell groups can be identified, including a dorsal nucleus of the posterior commissure and nucleus lentiformis. A more ventrally situated nucleus called **nucleus pretectalis** is also present in crocodiles.

The nucleus lentiformis mesencephali of reptiles is well established as the homologue of the mammalian nucleus of the optic tract. As with mammals, this nucleus will thus be considered below in the section on the accessory optic system. The relationship of a number of the other pretectal nuclei of reptiles to the set of the anterior, posterior, and medial pretectal nuclei in mammals is less clear, and independent evolution within the sauropsid and mammalian lineages may have resulted in greater parcellation of the pretectal region in the former than in the latter.

While in mammals, pupillary constriction is mediated through the olivary pretectal nucleus and the parasympathetic Edinger-Westphal nucleus, a specific pretectal nucleus in reptiles that is homologous to the olivary pretectal nucleus (and the area pretectalis of birds, as discussed below) remains to be definitively identified. Its probable location is in the more caudal and medial part of the pretectal region. In at least some reptiles, such as turtles, constriction of the pupil occurs in response to increased ambient light and also in conjunction with focusing of the eye on a near object, similar to pupillary functions in mammals. As noted further below, some of the homologies of nuclei across amniotes that can be recognized presently include 1) the posterior nucleus and the dorsal nucleus of the posterior commissure of turtles with the lateral spiriform nucleus of birds and the posterior pretectal nucleus of mammals and 2) the ventral pretectal nucleus of turtles and lizards with the nucleus pretectalis of crocodiles and the subpretectal nuclear complex of birds.

In birds, pretectal nuclei similar to those in reptiles are present, although the nomenclature varies, and not all comparisons are clear. Most of these nuclei are shown in Figure 20-13. Three nuclei receive a heavy retinal input: **nucleus lentiformis mesencephali**, the **tectal gray**, and the **area pretectalis**. Nucleus lentiformis mesencephali is homologous to the nucleus of the optic tract of mammals. Therefore, as for mammals, we will discuss it below in the section on the accessory optic system of birds. The tectal gray lies caudal to nucleus lentiformis mesencephali, at the intermediate level shown in Figure 20-13, where it comprises two poles, one situated dorsally and one ventrally. These poles merge across the base of the tectum at a slightly more rostral level. It projects to the optic tectum. It may be the homologue of the tectal gray of turtles, which is likely present in other reptiles as well, but more information on connections in all of these taxa would help to establish the correspondence. A fourth nucleus, called **nucleus pretectalis diffusus**, lies rostral to the area pretectalis at the level of the caudal pole of nucleus rotundus. It

receives a sparser retinal input, and, like the tectal gray, it projects to the tectum.

Area pretectalis appears to be the homologue of the olivary pretectal nucleus of mammals. Its main projection is to the Edinger-Westphal nucleus, which provides the parasympathetic innervation for pupillary constriction. However, in contrast to the doubly redundant olivary pretectal-Edinger-Westphal connections in mammals, with bilateral retinal input to the olivary pretectal nucleus and bilateral olivary pretectal projections to the Edinger-Westphal nucleus, the comparable pathways in birds are not redundant at all. In birds, the retinal fibers decussate entirely at the optic chiasm, so that the input to the diencephalic visual nuclei and optic tectum is entirely contralateral. The projection from the area pretectalis to the Edinger-Westphal nucleus is entirely contralateral as well. Thus, each Edinger-Westphal nucleus receives only input from the ipsilateral eye. Shining a light in a pigeon's eye will cause constriction of that same pupil but not both pupils as it would in mammals.

Nucleus pretectalis, which lies lateral to the area pretectalis, is remarkable for its reciprocal connections with the optic tectum combined with a lack of direct retinal input. Within the tectum, it terminates in layer 5b, which is the major input layer for retinotectal fibers. Its set of connections contrasts with that of the retinorecipient pretectal nuclei, including the area pretectalis, pretectalis diffusus, and the tectal gray, which project to the tectum but terminate in layers deep to the retinal input zone. In addition to its reciprocal tectal connections, nucleus pretectalis receives basal ganglia input, which is relayed to it from the globus pallidus via the posterior nucleus of the ansa lenticularis (Fig. 20-13). The latter nucleus contains GABAergic neurons, like those of the substantia nigra pars reticulata, which project directly to the tectum in both birds and mammals. A homologous posterior nucleus of the ansa lenticularis also has been identified in lizards, in which it projects to nucleus rotundus as well as to the tectum. However, the homologue in mammals of the posterior nucleus of the ansa lenticularis has not been established. Also, while some suggestions of homology of nucleus pretectalis with nuclei in reptiles and mammals have been made, its identity in this regard remains unclear.

Several more ventrally lying nuclei are present in the pretectal region of birds (Fig. 20-13), two of which are **nucleus subpretectalis** and **nucleus interstitio-pretectalis-subpretectalis**. These two nuclei are collectively called the **subpretectal complex**. They are reciprocally connected with nucleus rotundus in the dorsal thalamus, and the afferent pretectorotundal part of this loop is known to be GABAergic. The subpretectal complex in birds also projects to the avian nucleus pretectalis. Based on its total pattern of connections, the subpretectal complex may be involved in the shift of attention between eyes as well as in the local control of visual processing through nucleus rotundus. It is homologous to nucleus pretectalis in crocodiles and to the ventral pretectal nucleus in lizards and turtles. These nuclei in reptiles also are connected reciprocally with nucleus rotundus, and the component of the loop that is afferent to nucleus rotundus is likewise GABAergic.

The lateral and medial spiriform nuclei also lie within the pretectal region. The **lateral spiriform nucleus** relays inputs

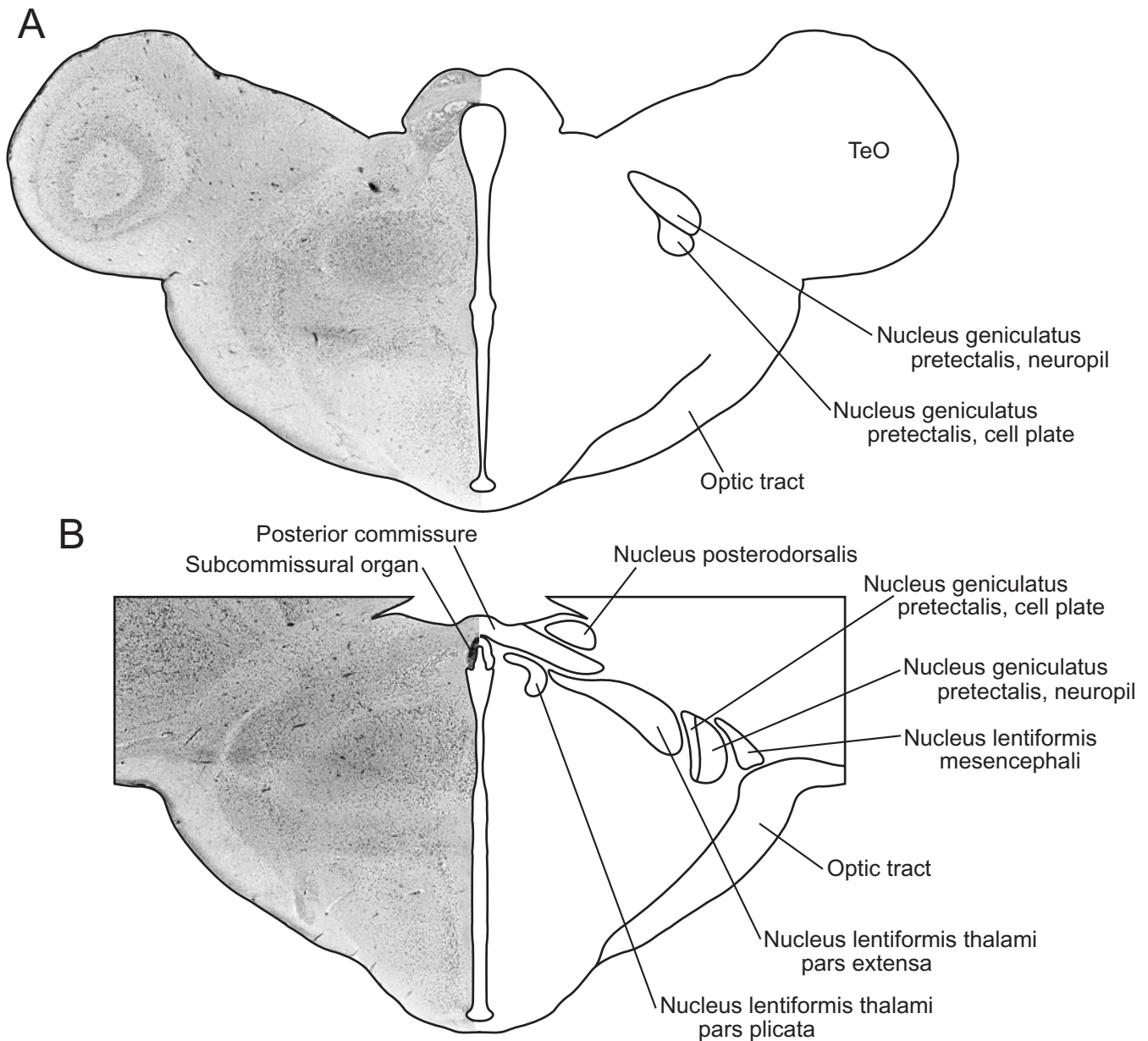


FIGURE 20-12. Transverse hemisections with mirror-image drawings through the pretectum of a lizard (*Iguana iguana*) in rostral-to-caudal order as A to D. Adapted from Butler and Northcutt (1973).

from the globus pallidus to the deeper layers of the optic tectum (see Chapter 24) and is the apparent homologue of the posterior nucleus and the dorsal nucleus of the posterior commissure of turtles. These nuclei in sauropsids also may be homologous to the posterior pretectal nucleus of mammals, which likewise receives pallidal inputs and projects to the optic tectum (superior colliculus), although as noted above, this comparison is tenuous.

The **medial spiriform nucleus**, in contrast, receives inputs from the telencephalic pallium, specifically the Wulst, dorsolateral corticoid area, and part of the arcopallium. It proj-

ects directly to the cerebellar cortex. Within the cerebellum, the medial spiriform axons terminate as mossy fibers and thus resemble the cerebellar inputs in mammals from pontine nuclei (rather than those from the inferior olivary nucleus, which are climbing fibers—see Chapter 14). Birds have a small, medially lying pontine nucleus that projects to the cerebellum, but it is minor in comparison to the pontine nuclei of mammals. Pontine nuclei have not been identified in reptiles at all, although crocodiles may have a homologue of the medial spiriform nucleus that is called **nucleus circularis**. It lies in the medial part of the pretectal region and projects to the cerebellum. In contrast,

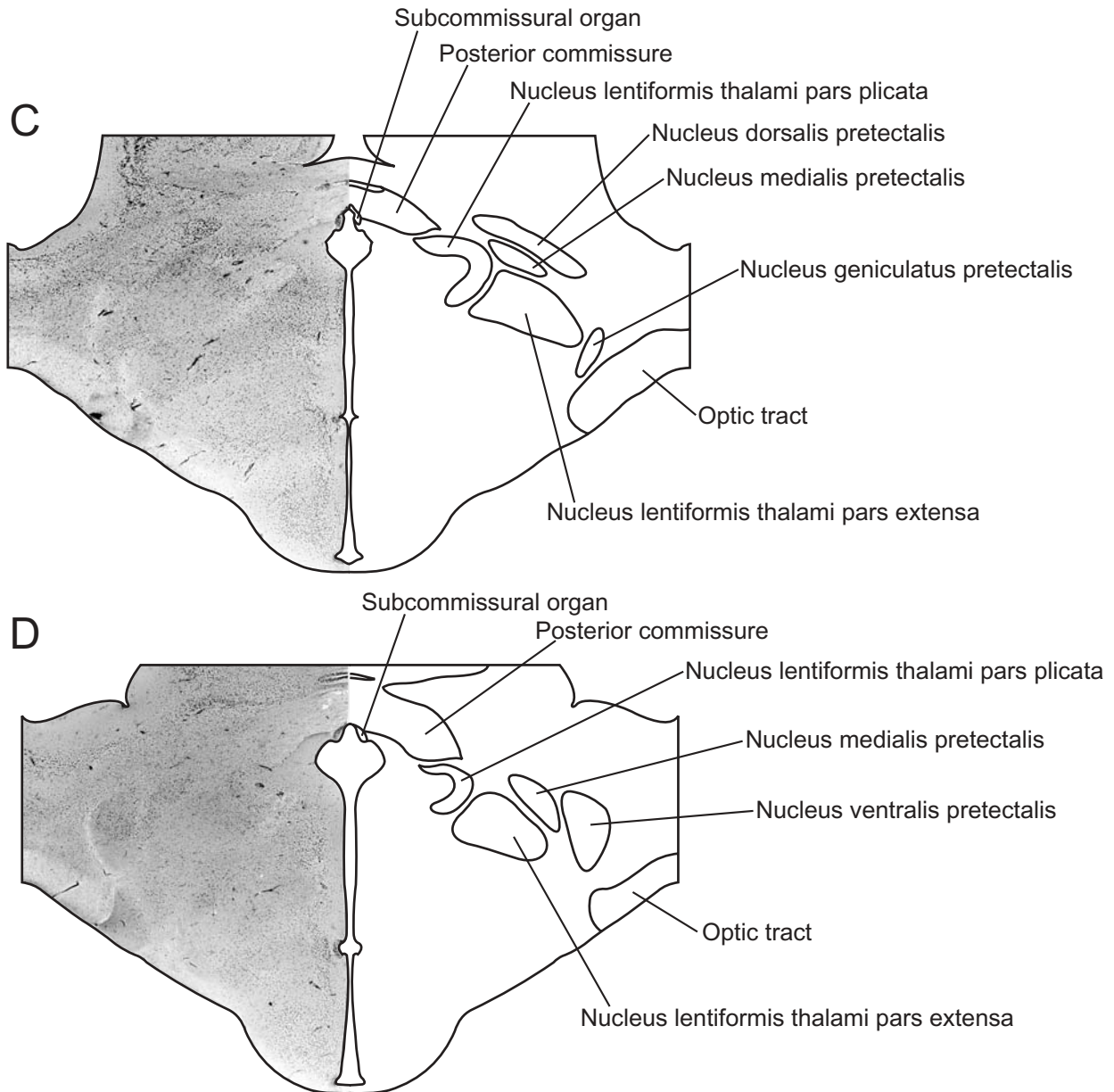


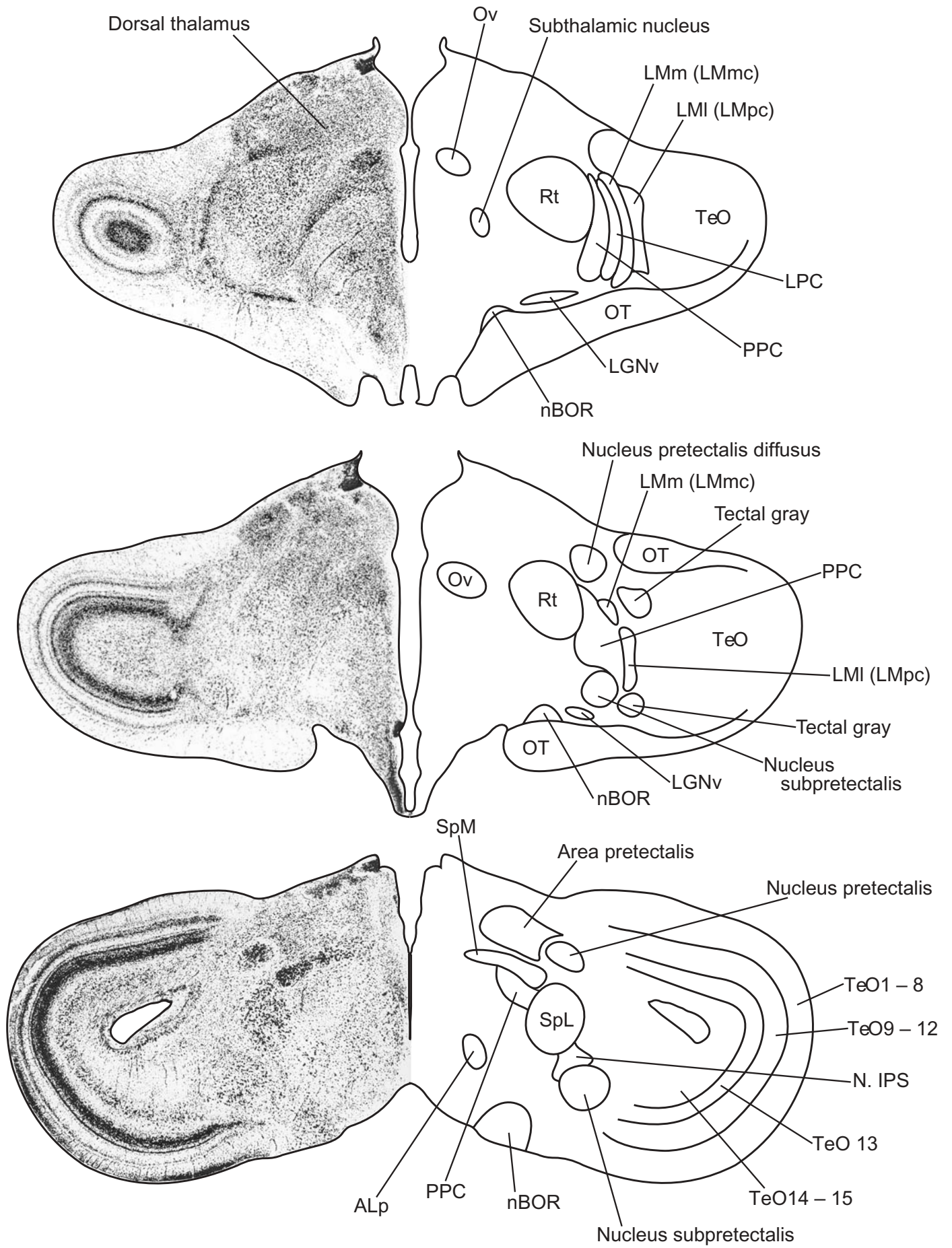
FIGURE 20-12. (Continued)

mammals lack a direct pretecto-cerebellar projection system. The medial spiriform nucleus of birds and nucleus circularis of crocodiles thus appear to be analogous to the pontine relay system of mammals but, due to the location of the nucleus in the pretectal region, probably not homologous to it.

ACCESSORY OPTIC SYSTEM

The movements of images across an animal's retina affect visuomotor behaviors, some of which are critical for survival. Such movements may be very similar whether they are pro-

duced (1) by the animal itself moving through a stationary space, (2) by movement of the animal's eyes while the animal is stationary, or (3) by movements of objects in the environment while both animal and eyes are stationary. Similar visual stimuli also result when the animal (stationary or moving) visually tracks an object, keeping the object's image in approximately the same location on the retina. Each of these similar retinal images may call for a different response; the visual system must therefore distinguish among them and send appropriate signals for action to the motor system in each case. Both pretectal and accessory optic structures make critical contributions to the solution of this problem.



The accessory optic system is a set of nuclei that is involved in regulating movements of the eyes in relation to the visual world. This system plays an important role in differentiating perceptual situations such as those listed above. It keeps an image stable on the retina as the eyes move, and it helps the animal to differentiate retinal image movement due to the animal moving from retinal image movement due to the object moving.

In teleosts, the functional partnership between the accessory optic nuclei and many of the pretectal nuclei is based on the common feature of a projection to the cerebellum and thence to oculomotor nuclei and the vestibular system. The cerebellar projections of the pretectal nuclei in teleosts, which are present in addition to the projections discussed above, as well as the similar projections of the accessory optic nuclei, will be discussed together here. Direct cerebellar projections from pretectal and/or accessory optic nuclei also are present in some but not all amniotes. Variation in the connections of these nuclei occurs to a marked degree in the different radiations of vertebrates.

The pretectal and accessory optic nuclei are involved in regulating movements of the eyes. A repeating pattern of eye movements, called **optokinetic nystagmus** (OKN), can be evoked by exposing an animal to patterns, such as black and white stripes, that are continuously moved across the visual field. The eyes first track the movement of the pattern in its direction and then return with a **saccade** (rapid movement) to fix on the next part of the pattern entering the visual field. The OKN is related to the processes of visual tracking and discriminating target movement from observer movement. Pretectal nuclei projecting to the cerebellum appear to be involved in OKN in the horizontal plane, while the accessory optic nuclei are involved in OKN in the vertical plane.

In most nontetrapod vertebrates, two accessory optic nuclei, dorsal and ventral, are present. These nuclei lie in the tegmentum and receive a retinal projection. Their functional interrelationship with the pretectum has been studied primarily in teleosts. In amphibians, reptiles, and birds, a single accessory, or basal, optic nucleus is present, in contrast to the three accessory optic nuclei present in mammals.

Group I

In lampreys, only a sparse retinal projection is present to the lateral part of the tegmentum. In squalomorph sharks,

retinal projections terminate in two sites in the tegmentum (Fig. 20-14). The more dorsal site is an unnamed neuropil area ventral to the intercollicular nucleus. The more ventral site is called the **basal optic nucleus**. In three of the four radiations of nonteleost ray-finned fishes, only one tegmental retinal target is present, the **basal** (or ventral accessory) **optic nucleus**. In *Amia* as in teleosts, as we will discuss below, two accessory optic nuclei, dorsal and ventral, are present (Fig. 20-3).

In amphibians, a single basal optic nucleus is present that lies in the lateral part of the tegmentum (Fig. 20-4). This nucleus is usually referred to as the **nucleus of the basal optic root** (nBOR), in reference to the fascicle (or root) of optic fibers that innervates it. The nBOR receives a substantial retinal projection and has reciprocal connections with nucleus lentiformis mesencephali. It projects to the medial part of the tegmentum and to the oculomotor (III) and trochlear (IV) nuclei. Dendrites of the nucleus of the medial longitudinal fasciculus extend into nBOR and can thus relay information to the vestibular system and spinal cord. A projection from nBOR to the cerebellum is very sparse, if present at all. Similarly, pretectal nuclei do not project to the cerebellum in amphibians.

Nucleus lentiformis mesencephali projects reciprocally to the optic tectum and to nBOR, as well as to more caudal sites in the brainstem, including the ventral part of the hindbrain and the abducens (VI) oculomotor nucleus. As noted above, it receives a substantial retinal input and also receives input from the optic tectum and the dorsal thalamus. Based on its location and pattern of both afferent and efferent connections, the nucleus lentiformis mesencephali of amphibians is considered to be homologous to the nucleus of the same name in sauropsids and to the nucleus of the optic tract of mammals, both of which are discussed below. Correspondingly, the amphibian nBOR is homologous to the nucleus of the same name in sauropsids and to the medial terminal nuclei of mammals, also discussed below.

The roles of the pretectal and accessory optic nuclei in visuomotor behaviors have been studied in amphibians in some detail. The regulation of eye movements in prey and predator detection, the detection of stationary objects such as barriers to escape, and the stabilization of gaze are among the functions of these nuclei. Nucleus lentiformis mesencephali is particularly involved in horizontal optokinetic nystagmus—conjugate movement of the eyes in the horizontal plane to allow fixation of the gaze on moving objects.

FIGURE 20-13. Transverse hemisections with mirror-image drawings through the pretectum of a bird (*Columba livia*). The most rostral section is at the top. The overlying telencephalon is not shown. Most pretectal nuclei are shown as well as some additional nuclei for orientation, such as nuclei rotundus (Rt) and ovoidalis (Ov) of the dorsal thalamus and the ventral lateral geniculate nucleus (LGNv), a component of the ventral thalamus. Additional abbreviations: ALp, posterior nucleus of the ansa lenticularis; LMI (LMpc), nucleus lentiformis mesencephali pars lateralis (LM pars parvocellularis); LMm (LMmc), nucleus lentiformis mesencephali pars medialis (LM pars magnocellularis); LPC, nucleus laminaris precommissuralis; nBOR, nucleus of the basal optic root; N. IPS, nucleus interstitio-pretecto-subpretectalis; OT, optic tract; PPC, nucleus principalis precommissuralis; SpL, nucleus spiriformis lateralis; SpM, nucleus spiriformis medialis; TeO, optic tectum; TeO 1–8, etc., layers of the optic tectum. Adapted from Karten and Hodós (1967) with some nomenclature based on Gamlin and Cohen (1988) and used with permission of The Johns Hopkins University Press.

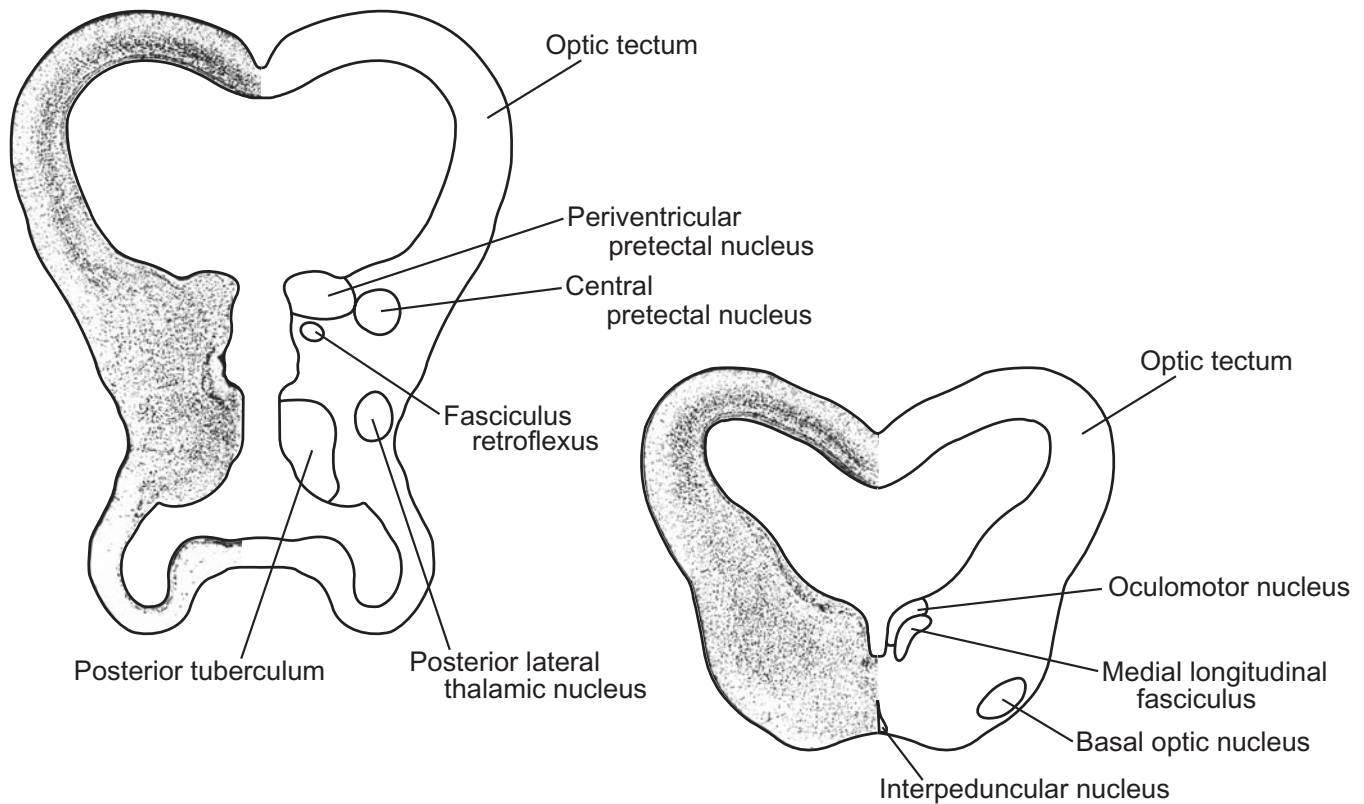


FIGURE 20-14. Transverse hemisections with mirror-image drawings through the midbrain of a shark (*Squalus acanthias*). The more rostral section is at the top left. Adapted from Northcutt (1979) and used with permission of Elsevier.

Group II

Anamniotes. In hagfishes, no retinal projections have been traced to the tectum. Retinal projections terminate in the pretectum as discussed above. In galeomorph sharks, two accessory optic nuclei have been found, one near the intercollicular nucleus and one more caudal and ventral at the level of the oculomotor nucleus. Only the former of these two nuclei has been found in a skate.

In teleosts, both **dorsal** and **ventral accessory optic nuclei** are present (Fig. 20-7). The connections of the accessory optic nuclei and the pretectum with the cerebellum and other brainstem sites are extensive in comparison with other anamniote vertebrates. These pathways are diagrammed in Figure 20-15. The nuclei that receive retinal and/or tectal inputs are indicated in the figure. Four of the nuclei also project to the optic tectum—the central pretectal nucleus, the dorsal periventricular pretectal nucleus, the ventral periventricular pretectal nucleus, and the dorsal accessory optic nucleus—and other feedback circuits also exist.

As shown in Figure 20-15, the parvocellular superficial pretectal nucleus projects directly to the trochlear nucleus (IV) and is the only pretectal nucleus known to project to any of the oculomotor nuclei. The parvocellular superficial pretectal nucleus does not project to the cerebellum, however. Of all the

pretectal and accessory optic nuclei, only the dorsal accessory optic nucleus projects to both an oculomotor nucleus (III in this case) and to the cerebellum. In the superficial pretectal zone, the magnocellular superficial pretectal nucleus projects either to nucleus isthmi (in percomorphs) or nucleus lateralis valvulae (in goldfishes), as discussed in detail above. Both the latter nuclei project, in turn, to the cerebellum. The central pretectal nucleus, the dorsal periventricular pretectal nucleus, and, where present, the paracommissural nucleus, project to the cerebellum, as does the ventral accessory optic nucleus.

The cerebellum (see Chapter 14) projects to oculomotor nuclei and to the nucleus of the medial longitudinal fasciculus, which is interconnected with the vestibular system. Hence, these multiple pathways allow visual input to be integrated with vestibular information. The motor output of the pretectal-accessory optic system is involved in smooth pursuit movements of the retina to track a moving image. Output to the motor systems of the body, such as that from the parvocellular superficial pretectal nucleus to the raphe and thence to the spinal cord, would allow for tracking of an image as well by movements of the head and body. Outputs to the inferior lobe of the hypothalamus from the posterior pretectal nucleus (or the intermediate superficial pretectal nucleus/nucleus glomerulosus in euteleosts) play a role in orientation and

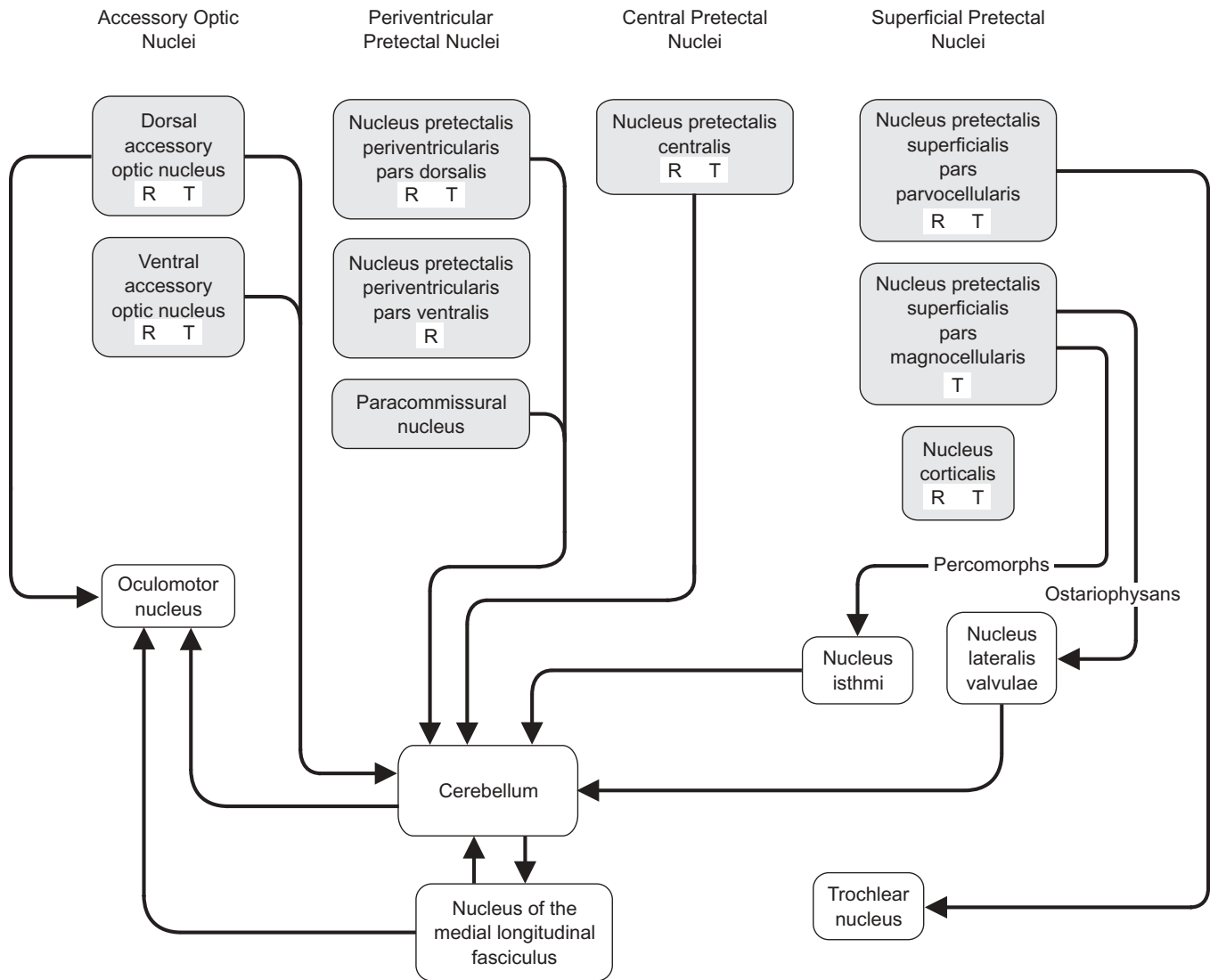


FIGURE 20-15. Diagram of pathways through the accessory optic nuclei and pretectal nuclei to the cerebellum and oculomotor nuclei in teleosts. Retinorecipient and/or tectorecipient nuclei are indicated by the letter(s) R and/or T, respectively, in a white box underneath the name of each nucleus. The oculomotor nuclei and cerebellum also receive inputs from the vestibular system.

feeding responses, although further work on the efferent pathways is needed.

Mammals. Mammals have three accessory optic nuclei, called the **dorsal**, **lateral**, and **medial terminal nuclei** (Fig. 20-10), all of which receive retinal projections, as well as some inputs from association visual cortical areas. Recent work has confirmed that all mammals have all three nuclei, despite earlier reports of the possible absence of part or all of the medial terminal nucleus in rhesus monkeys. The dorsal terminal nucleus (**DTN**) and the nucleus of the optic tract of the pretectum are now grouped as the **NOT-DTN complex**, since they are anatomically contiguous and share similar retinal inputs. They also both receive inputs from a variety of visual

cortical areas, including primary visual cortex and visual association cortical areas, particularly some of those concerned with motion detection. Likewise, both NOT and DTN project to part of the inferior olivary nucleus, specifically to its dorsal part, called the **dorsal cap of Kooy**. Projections of the NOT have been studied in some depth and found to arise from different sets of neuron populations within it. In addition to projecting to the lateral terminal nucleus and to the dorsal cap of the inferior olivary nucleus, NOT gives rise to separate projections to the dorsal lateral geniculate nucleus and the lateral posterior-pulvinar complex. The projections to the dorsal lateral geniculate nucleus are GABAergic and thus inhibitory, while those to the lateralis posterior-pulvinar complex are glutamatergic and thus excitatory. NOT also projects to the nucleus of Bechterew, which, as noted above, is an accessory

oculomotor nucleus that similarly projects to the inferior olivary nucleus.

The lateral terminal nucleus projects to the olivary pretectal nucleus, which is involved in pupillary constriction as discussed above. Most of its outputs are related to the control of eye movements, however. It is reciprocally connected with the NOT, and it projects to several of the accessory oculomotor nuclei—the **nucleus of the posterior commissure**, and, like some of the pretectal nuclei discussed above (Fig. 20-11), the interstitial nucleus of Cajal, nucleus of Darkschewitsch (Fig. 20-10), and the nucleus of Bechterew—all of which influence the oculomotor nuclear complex and its control of eye movements, directly and/or via the cerebellum and vestibular system as discussed above. Further, the lateral terminal nucleus projects to the reticular formation, the dorsolateral pontine nucleus, the vestibular nuclei, and the medial terminal nucleus. The medial terminal nucleus also projects to the vestibular nuclei. Thus, the descending pathways from these accessory optic nuclei are highly similar to those of the anterior, medial, and posterior pretectal nuclei in their influence on the vestibulo-ocular system.

Additionally, the accessory optic system is reciprocally connected with retino-recipient components of the ventral thalamus. All three of the accessory optic nuclei project to a part of the ventral thalamus called the **intergeniculate leaflet** (see Chapter 19), and the latter nucleus gives rise to reciprocal projections back to the dorsal and lateral terminal nuclei, as well as to the nucleus of the optic tract and the olivary pretectal nucleus. The ventral lateral geniculate nucleus is also involved in this circuitry. Thus, the ventral thalamus contributes to the vestibular-visuomotor system.

Along with the nucleus of the optic tract, the accessory optic nuclei are crucial for the optokinetic reflex. The analysis of incoming visual information is distributed among the nuclei such that the nucleus of the optic tract and the dorsal terminal nucleus contain neurons that respond best to large, horizontally moving stimuli, while the lateral and medial terminal nuclei contain neurons that are most interested in vertically moving stimuli. In response to any slip of the visual input across the retina, the accessory optic nuclei orchestrate eye movements to compensate, thus maintaining the image as a stationary object.

Reptiles and Birds. In reptiles, a single **nucleus of the basal optic root (nBOR)** is present in the lateral part of the tegmentum. It receives retinal and tectal inputs, as well as additional visual reciprocal connections with the second component of the accessory optic system, nucleus lentiformis mesencephali. The nucleus of the basal optic root projects to the granular layer of the cerebellum. However, unlike its homologue of the same name in birds and the medial and lateral terminal nuclei in mammals, nBOR in turtles recently has been found to lack projections to other brainstem sites, including the vestibular and accessory oculomotor nuclei. In addition to its reciprocal connections with the nucleus of the basal optic root, nucleus lentiformis mesencephali receives a direct retinal fiber input. It contains GABAergic neurons that project to the dorsal lateral geniculate nucleus in the dorsal thalamus, corresponding to similar a GABAergic pathway that originates from its homologue in mammals, the nucleus of the optic tract.

In birds (Fig. 20-13), the nucleus of the basal optic root is also present and previously was called nucleus ectomamillaris. It is considered to be the homologue of the medial and lateral terminal nuclei of mammals. In birds with frontally placed eyes, such as owls, a high proportion of nBOR neurons are binocularly responsive, as is the case in many mammals with frontally placed eyes. The high proportion of binocular neurons has evolved independently in these two groups in correlation with frontal vision and the utilization of depth cues in retinal image stabilization. In pigeons, nBOR is thought to play a major role in the control of head bobbing. The nucleus of the basal optic root receives inputs from both the retina and the visual Wulst, the homologue of mammalian striate cortex. Within the retina, the cells that project to nBOR are referred to as **displaced ganglion cells** due to their location outside the main ganglion cell layer. The nucleus of the basal optic root has rather extensive efferent projections that include descending projections to the inferior olivary nucleus and pontine nuclei, accessory oculomotor nuclei such as the nucleus of Darkschewitsch and interstitial nucleus of Cajal, the general somatic, main oculomotor nuclear complex, and vestibular and cerebellar nuclei. The nucleus of the basal optic root also projects to nucleus lentiformis mesencephali in the pretectum.

The nucleus lentiformis mesencephali of birds, as noted above, is the homologue of the nucleus of the optic tract of mammals. It can be subdivided into a **pars medialis** (alternatively called the pars magnocellularis) and a **pars lateralis** (alternatively called the pars parvocellularis). The cells of this nucleus participate along with nBOR in producing the optokinetic response to moving stimuli such that compensatory eye movements are made that allow stabilization of the image on the retina. The pars medialis neurons respond better to moving stimuli of slower velocity, while the pars lateralis neurons prefer faster velocities.

Nucleus lentiformis mesencephali receives retinal projections and also input from the visual Wulst. It projects to nBOR, just as the NOT projects to the medial and lateral terminal nuclei in mammals, and it also projects to the dorsolateral thalamus and the inferior olivary nucleus, similar to the projections of NOT in mammals. The projections of nucleus lentiformis mesencephali to the dorsal thalamus involve multiple sites of termination, including the avian homologue of the dorsal lateral geniculate nucleus. The lentiformis mesencephali projections to the DLGN are GABAergic in birds, as are the NOT projections to it in mammals. Thus, the lentiformis mesencephali-dorsal thalamic projection includes projections specifically equivalent to the NOT-DLGN pathway in mammals. This pathway may contribute to the bird's ability to distinguish the motion of objects from its own motion. Unlike the situation in mammals, projections to the dorsal thalamus also arise from nBOR. Its main part gives rise to a modest projection to nucleus rotundus, and a dorsal subdivision of the nucleus projects substantially to the dorsal lateral geniculate nucleus.

EVOLUTIONARY PERSPECTIVE

The pretectum is better differentiated in teleost fishes than in any other group of vertebrates. Among amniotes, it is better differentiated, that is, more elaborated, in reptiles and birds

than in placental mammals and may have been secondarily reduced in monotremes. The number of accessory optic nuclei varies across vertebrate taxa. Lampreys and all jawed vertebrates have at least one accessory optic nucleus. Most cartilaginous fishes have two, as do *Amia* and teleosts among ray-finned fishes. Reptiles and birds both have two accessory optic nuclei, whereas mammals have four, including the nucleus of the optic tract; the four nuclei in mammals can be combined into two groups that are respectively homologous to the two nuclei present in sauropsids (the medial and lateral terminal nuclei to nBOR and the dorsal terminal nucleus-NOT to nucleus lentiformis mesencephali). Whether nBOR and nucleus lentiformis mesencephali are homologous to the two accessory optic nuclei present in many anamniotes has not yet been definitively established, although it seems likely.

In teleosts, the pretectal nuclei are characterized by reciprocal connections with a number of structures and by other multisynaptic, feedback pathways. These nuclei influence motor behavior via major efferent pathways to the hypothalamus, through the raphe to the spinal cord, to the oculomotor nuclei, and to the cerebellum.

Among amniotes, some discrete homologies can be recognized between pretectal and accessory optic nuclei across taxa, while other nuclei cannot yet be so characterized. An oversimplified diagram (Fig. 20-16) summarizes the major similarities and differences between mammals and sauropsids (using the nomenclature of birds for the latter). Many of the major connections of these various nuclei that are discussed and/or diagrammed elsewhere in this chapter and on which many of the homologies are inferred are not included for the

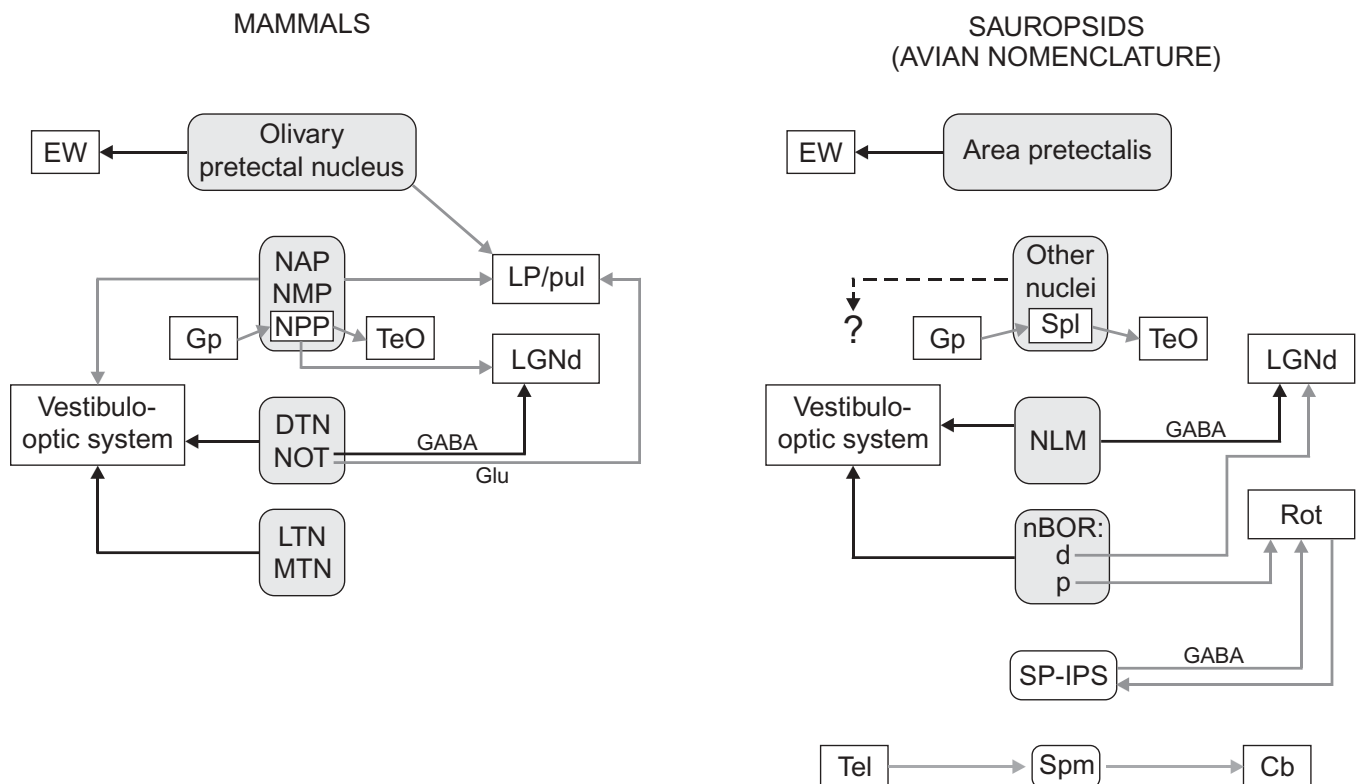


FIGURE 20-16. Comparison of some of the main connections of the divisions/nuclei of the pretectum across amniotes. For sauropsids, structures common to both reptiles and birds are included, but only avian nomenclature is used. Many connections described elsewhere are not included for the sake of making a relatively simplified comparison. Similar relative position in the diagram is used in most cases to indicate homologous nuclei or groups of nuclei. Black arrows indicate connections present in both mammals and sauropsids between homologous structures. Gray arrows indicate connections currently identified in only one group or the other and/or that may not be homologous. Abbreviations: Cb, cerebellum; DTN, dorsal terminal nucleus; EW, Edinger-Westphal nucleus; GABA, γ -aminobutyric acid; Glu, glutamate; Gp, globus pallidus; LGNd, dorsal lateral geniculate nucleus; LP/pul, nucleus lateralis posterior/pulvinar; LTN and MTN, lateral and medial terminal nuclei, respectively; NAP, NMP, and NPP, anterior, medial, and posterior pretectal nuclei, respectively; nBOR, d and p, nucleus of the basal optic root, dorsal and principal (main) parts; NLM, nucleus lentiformis mesencephali; NOT, nucleus of the optic tract; Rot, nucleus rotundus; SP-IPS, nuclei subpretectalis and interstitio-pretectalis-subpretectalis; Spl, nucleus spiriformis lateralis; Spm, nucleus spiriformis medialis; Tel, telencephalon; TeO, optic tectum.

sake of highlighting the differences, most of which involve pretectal and accessory optic system projections to the dorsal thalamus.

Within the pretectum, the olivary pretectal nucleus of mammals and the area pretectalis of birds, both of which project to the Edinger-Westphal nucleus, appear to be homologous, although the corresponding nucleus has yet to be identified in reptiles. The bilateral olivary pretectal projections in mammals contrast with the solely contralateral projections in birds. Since an olivary pretectal nucleus is present in amphibians, at least as identified in a salamander, and gives rise to bilateral projections to the parasympathetic oculomotor division, this bilateral pattern was probably present in at least the earliest tetrapods (or prototetrapods) if not earlier.

In mammals, the three remaining nuclei considered here as pretectal—the anterior, medial, and posterior pretectal nuclei—cannot be compared for the most part as discrete homologues of the various pretectal nuclei in reptiles and birds. Of the latter, the posterior pretectal nucleus of mammals resembles the nucleus spiriformis lateralis of birds and the homologous nuclei in reptiles in its relay of globus pallidus input to the optic tectum, as indicated in Figure 20-16, but its other connections and its position argue against this relationship. The pretectal relay of pallidal inputs to the tectum thus may have evolved separately in mammals and sauropsids. The presence of such projections in amphibians indicates that they were probably present in ancestral tetrapods. If the particular pretectal cell group in the pathway is indeed different in sauropsids and mammals, this variation may have resulted from differential parcellation of the pretectal region in the two amniote lines. Whether a pallidopretectal relay system is present in fishes remains to be determined.

The accessory optic system shows a relatively conservative evolutionary pattern, at least within tetrapods. The nucleus of the basal optic root of amphibians and sauropsids appears to be homologous to the lateral and medial terminal nuclei of mammals, and the nucleus lentiformis mesencephali of sauropsids and probably of amphibians is likewise homologous to the nucleus of the optic tract-dorsal terminal nucleus complex of mammals. However, some connections of these nuclei, particularly in terms of ascending projections to the thalamus, have evolved independently within the sauropsid line. Likewise, as one consequence of the greater parcellation of the pretectal region seen in sauropsids, the subpretectal nuclear complex of birds and its homologue in reptiles may be unique to this amniote line.

Direct cerebellar projections from pretectal and accessory optic nuclei are a further example of independently acquired pathways. They are present in two major groups of vertebrates, teleost fishes and sauropsids. On the basis of current data, one must hypothesize that such cerebellar projections are apomorphic and were evolved independently in these two groups. As we will discuss in Chapter 22, placental mammals have the most highly differentiated and elaborate dorsal thalamus among the various radiations of vertebrates. In contrast, the pretectum and its associated accessory optic system are most highly differentiated and elaborated in teleosts, and, among amniotes, these sets of nuclei are also relatively better developed in sauropsids than in mammals. As we discuss below, teleosts also have migrated pregglomerular nuclei that relay sensory infor-

mation to the telencephalon and have no counterpart in mammals.

MIGRATED POSTERIOR TUBERCULUM

We have already encountered the unmigrated part of the posterior tuberculum in the tegmentum (Chapter 17). As described there, it lies in the medioventral part of the tegmentum, and some of its cells contain dopamine. The current evidence strongly supports the idea that the posterior tuberculum is homologous as a field to the caudal diencephalic (A11) and rostral tegmental (rostral A9/A10) dopaminergic cell groups of mammals.

In most ray-finned fishes, migrated nuclei of the posterior tuberculum have been identified. The largest of these nuclei, the pregglomerular nuclear complex, relays sensory information to the telencephalon. The pathways through the pregglomerular nuclear complex mimic sensory relay pathways through the dorsal thalamus in their organization.

At least one migrated nucleus is also present in this caudal region of the diencephalon in cartilaginous fishes and will be discussed here. This nucleus has connections that are similar to some of the connections of the pregglomerular nuclear complex of teleost fishes and may be homologous as a field to it.

Group I

Migrated nuclei of the posterior tuberculum are not present in some of the Group I animals with laminar brains. In squalomorph sharks, a nucleus called the **posterior lateral thalamic nucleus** is present lateral to the periventricular part of the posterior tuberculum (Fig. 20-2). This nucleus is known to receive an electrosensory input in skates and rays. In a squalomorph shark, it has been found to project to the medial pallium in the telencephalon. In cladistian ray-finned fishes, a nucleus medianus of the posterior tuberculum has been identified; it appears to relay visual inputs from the optic tectum to the distal, more everted part of the pallium in the telencephalon, a pathway that may be unique to this basal ray-finned fish taxon. In gars and *Amia*, a **preglomerular nuclear complex** is present lateral to the posterior tuberculum (Fig. 20-3).

Group II

In hagfishes, a relatively large nucleus called the **area lateralis of the posterior tuberculum** has been identified, but its connections remain to be studied. In Group II cartilaginous fishes, the **posterior lateral thalamic nucleus** (also called the **central thalamic nucleus**) lies lateral to the periventricular part of the posterior tuberculum (Fig. 20-6) and receives an electrosensory input. Both the latter nucleus and the posterior tuberculum project to the medial pallium in the telencephalon.

In teleosts, several migrated nuclei of the posterior tuberculum are present, the largest and most prominent of which is actually a group of nuclei that form the **preglomerular nuclear complex** [Fig. 20-17 and compare with Fig. 20-

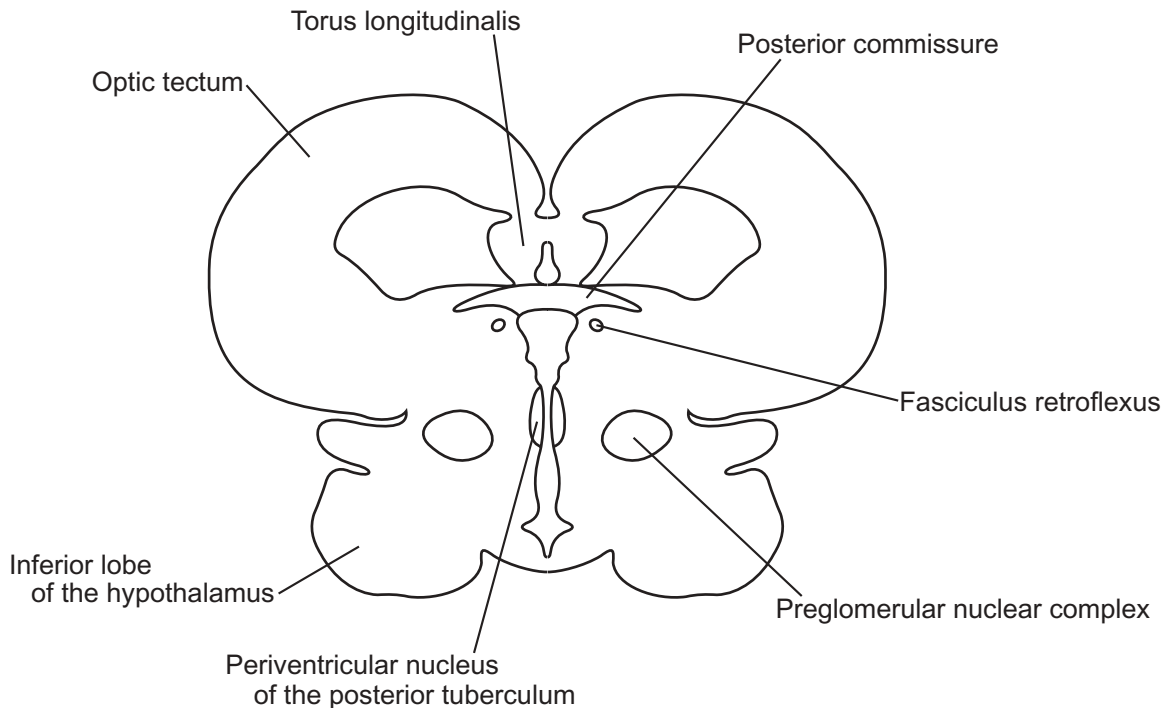


FIGURE 20-17. Drawing of a transverse section through the posterior tuberculum of a teleost (*Lepomis cyanellus*). Adapted from Butler et al. (1991) and used with permission of S Karger AG, Basel.

9(K,M)]. One note of caution needs to be made concerning the terminology for this cell group: it has become quite uniform across the literature over the past decade, but, in earlier literature, many different terms were applied to it or to its various components. These previous terms include nucleus prethalamicus, nucleus rotundus, thalamus, and nucleus glomerulosus, and there is a similar array of terms for nucleus glomerulosus of the pretectum, which we discussed above. These terms have also been used for other nuclei in neighboring regions of the brain in other species. Thus, in reading the earlier literature, the identity of any nucleus in this region must be determined by the content of the particular paper, such as comments on the connections and location of the nucleus and on the terms others have used for it.

The cytoarchitecture and degree of development of the preglomerular nuclear complex varies among different species of teleosts. Boundaries between nuclei within the complex are not consistently easy to recognize, but lateral, medial, and various other divisions can be distinguished. The preglomerular nuclear complex is mostly involved with the relay of ascending sensory pathways to the telencephalon, but it has a substantial number of other, nontelencephalic connections and is also involved in some descending pathways. For example, in two osteoglossomorph taxa, the freshwater butterfly fish *Pantodon buchholzi* and the weakly electroreceptive mormyrids, the dorsal part of the preglomerular nuclear complex relays descending inputs from the telencephalon to the cerebellum.

The major ascending sensory pathways that are relayed through parts of the preglomerular complex are those of the acoustic and lateral line systems and, in some taxa, the gusta-

tory system. While most teleosts have only a mechanosensory lateral line system, electroreception has been evolved independently in two groups of teleosts—some osteoglossomorphs (mormyrids, such as *Gnathonemus petersii*, and notopterids) and some ostariophysans (gymnotids, such as *Apteronotus leptorhynchus* and *Eigenmannia virescens*, and silurids, such as the channel catfish *Ictalurus punctatus*). Differences in the development and connections of the preglomerular nuclear complex reflect this evolutionary history.

In most teleosts, including electroreceptive teleosts, the mechanosensory lateral line input to the torus semicircularis is relayed to the lateral part of the preglomerular nuclear complex (PGL). Auditory projections to PGL have also been found in some teleosts. In at least some teleosts, both the lateral and medial parts of the preglomerular nuclear complex project to the pallium, in most taxa to the medial part of area dorsalis, Dm, but projections to more lateral parts of the pallium have also been found in some cases. The preglomerular nuclear complex also projects to the striatum [Fig. 20-18(A)]. In electroreceptive ostariophysans—silurids and gymnotids—additional ascending pathways through PGL are present. The electrosensory part of the torus semicircularis in electroreceptive ostariophysans does not project directly to PGL but to a nucleus in the region of the pretectum called **nucleus electrosensorius** [Fig. 20-18(B)]. This nucleus projects to PGL, which, in turn, projects to the pallium and striatum in the telencephalon. Nucleus electrosensorius also projects to the cerebellum.

In mormyrids and notopterids, the electroreceptive osteoglossomorphs, the preglomerular nuclear complex is markedly enlarged and has more subdivisions than in other

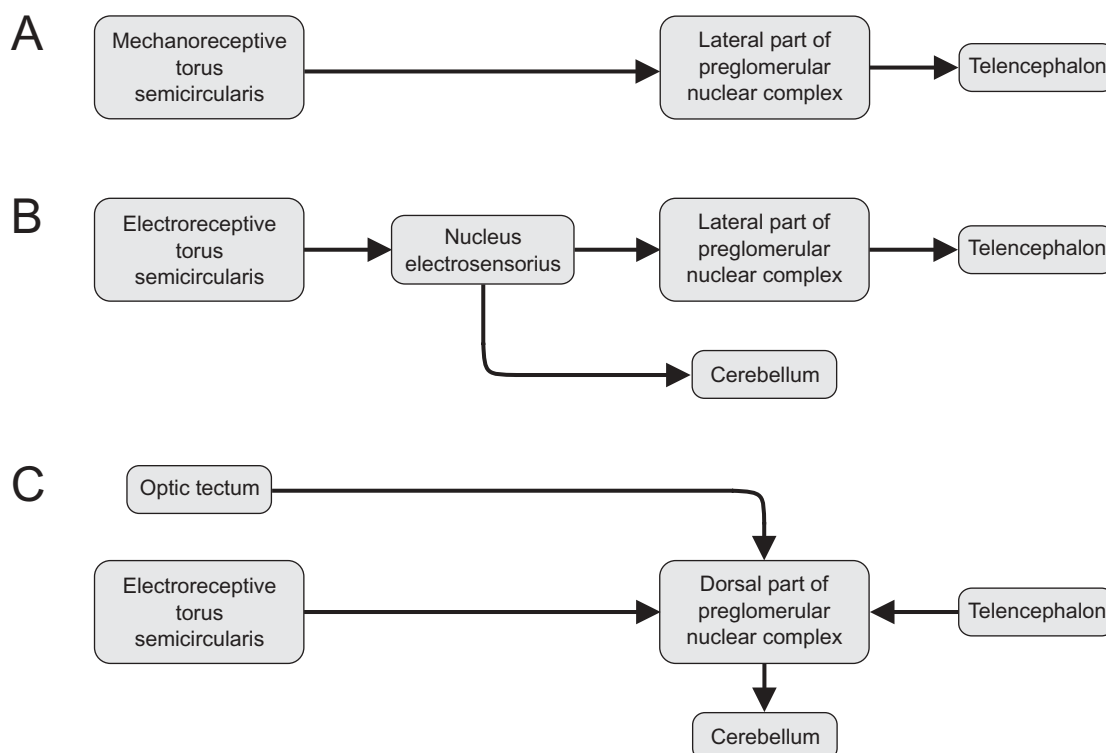


FIGURE 20-18. Diagram of some of the connections of the preglomerular nuclear complex. A: Connections present in most teleosts, including electroreceptive teleosts. B: Additional connections present in most electroreceptive teleosts. C: Connections of PGd present in the electroreceptive mormyrid teleosts.

teleosts. In mormyrids [Fig. 20-18(C)], the electroreceptive part of the torus semicircularis projects to a dorsal part of the preglomerular complex (PGd), which also receives inputs from the telencephalon and the optic tectum. Instead of projecting to the telencephalon, however, PGd projects to the cerebellum. Within the rest of the preglomerular nuclear complex, a ventral part (PGv) is the major source of ascending projections to the telencephalon. It receives acoustic and mechanosensory inputs from the torus semicircularis and relays the ascending information to the pallium; the PGv of mormyrids is recognized as the homologue of the PGI of ostariophysans. An anterior part of the preglomerular nuclear complex, PGa, also relays ascending mechanosensory inputs to the pallium.

In mormyrids and in some electroreceptive ostariophysans, the superficial pretectal and accessory optic nuclei are markedly reduced or absent. Electroreceptive inputs to the telencephalon and/or to the cerebellum have been selected for over the course of evolution in favor of visual pretectal/accessory optic pathways to the cerebellum. Five pretectal/accessory optic nuclei project to the cerebellum in most teleosts, including the common goldfish (an ostariophysan)—in addition to cerebellar projections from nucleus electrosensorius where present. Only two of five cerebellar pathways of most teleosts are well developed in mormyrids, but a new pathway to the cerebellum from PGd is present. This variation in electrosensory pathways is one of the more striking examples of the changes in nuclei and pathways that can occur in response to selective pressures.

In addition to relaying lateral line information to varying parts of the brain, the preglomerular nuclear complex relays gustatory information to the telencephalon in some taxa. The secondary gustatory nucleus receives gustatory input from the facial lobes (see Chapter 11); in sunfishes, the secondary gustatory nucleus has been found to project to part of the preglomerular nuclear complex, which in turn projects to the medial part of area dorsalis, Dm, in the telencephalon. In the sea robin, *Prionotus carolinus*, a percomorph euteleost fish, the lateral division of the preglomerular nuclear complex receives ascending chemosensory inputs from solitary chemosensory cells on the pectoral fin rays, relayed to it via the medial lemniscus, while gustatory inputs appear to be restricted to a more ventrolateral site bordering the complex and to another part of the complex called the **posterior thalamic nucleus**. In catfishes, the secondary gustatory nucleus projects to a nucleus called **nucleus lobobulbaris**, which lies just caudal to the major part of the preglomerular nuclear complex and is probably derived from it. Nucleus lobobulbaris projects to the medial part of the telencephalic pallium, Dm, as well as to its central part, Dc. In contrast, in goldfishes, as discussed in Chapter 11, the ascending gustatory pathway to the telencephalon via the preglomerular nuclear complex is somewhat indirect. The tertiary gustatory nucleus that lies within the preglomerular nuclear complex projects to the inferior lobe of the hypothalamus and to a structure called the torus lateralis (see Chapter 17), both of which project to the posterior thalamic nucleus, which serves as the

diencephalic relay to the telencephalon for the ascending gustatory pathway.

In most teleosts, the migrated nuclei of the posterior tuberculum include several additional, smaller nuclei in the vicinity of the pregglomerular nuclear complex. These smaller pregglomerular components include a caudally lying nucleus frequently called the mammillary body, as well as other nuclei such as nucleus subglomerulosus and the lateral thalamic nucleus. The latter nucleus is known to receive afferent fibers from the magnocellular superficial pretectal nucleus and the secondary gustatory nucleus and to project to the optic tectum in percomorph euteleosts. The posterior thalamic nucleus is another of the smaller pregglomerular components; it projects to the telencephalon, particularly in goldfishes, as noted for the ascending gustatory pathway in this taxon.

EVOLUTIONARY PERSPECTIVE

In amniote vertebrates, no migrated nuclei of the posterior tuberculum that relay ascending sensory information are present. Such migrated nuclei have been identified only in cartilaginous and ray-finned fishes. Whether the posterior lateral thalamic nucleus of cartilaginous fishes is homologous as a field to the pregglomerular nuclear complex of teleosts or whether these nuclei have been evolved independently and are an example of parallelism or convergence remains to be determined.

The pregglomerular nuclei in cartilaginous and ray-finned fishes appear to constitute an alternative to the dorsal thalamus as a relay of sensory information to the telencephalon. A marked degree of development of both the pregglomerular nuclear complex and the pretectal nuclei combined with minimal development of the dorsal thalamus characterizes many fishes. This condition contrasts with the reverse situation in amniotes—the absence of migrated, sensory-relay nuclei derived from the posterior tuberculum, only a moderately developed pretectum, and an extensively developed dorsal thalamus.

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21

Epithalamus

INTRODUCTION

The epithalamus does not vary in the degree of its development as a function of Group I versus Group II vertebrates. We will therefore discuss the structures of the epithalamus in the various radiations of vertebrates without separately considering Groups I and II.

The epithalamus (Fig. 21-1) can be divided into two parts. The first part is immediately dorsal to the dorsal thalamus and is composed of the **habenular nuclei** and any related nuclei (see Box 21-1). The second part is called the **epiphysis**. This part forms in the roof of the third ventricle between the habenula and the posterior commissure. It is composed of one or two components, the **pineal gland** and, in various taxa, a **parapineal organ**, a **parietal eye**, or a **frontal organ**. Fibers that originate from neurons within the epiphysis constitute the **epiphyseal nerve** (see Chapter 9), although they generally can be referred to as the **pineal tract** and/or the **parietal nerve**. The major functional roles of the epithalamus are the regulation of cyclic behavior, such as circadian rhythm and reproductive cycles, in response to the day-night cycle, and the modulation of other systems in the brain such as the limbic system, hypothalamus, raphe, and some motor-related pathways.

EPIPHYSIS

An epiphysis has not been identified in hagfishes. In lampreys and some jawed vertebrates, the epiphysis consists of two outgrowths from the roof of the third ventricle, called the pineal and parapineal organs, both of which have photo-

receptive cells. Where present, the parapineal organ is embryologically derived from the rostral part of the epiphysis and is located on the left side of the brain. It is attached to the left habenula to which it projects. Among jawed vertebrates, a parapineal organ has been found in trout and the coelacanth *Latimeria*. The parietal eye of lizards may also be a parapineal structure. A parapineal organ is absent in other taxa, however, including cartilaginous fishes, many bony fishes, and amphibians, and it is either absent or vestigial in mammals and birds. Based on its shared features, the parapineal organ/parietal eye structure may be syngenous across the taxa where it occurs, i.e., specified by the same patterning genes inherited from a common ancestor.

In lampreys, the parapineal organ is a rostral component of the epiphysis that is physically attached to the left habenula. It receives afferent input from several sites, including a lateral part of the telencephalic pallium, the pretectal area, and a nucleus in the rostral part of the diencephalon called the **subhippocampal-thalamic nucleus** (Fig. 21-2). The parapineal organ is reciprocally connected with the left habenula and also projects to the **interpeduncular nucleus** of the midbrain (see Chapter 16). The parapineal organ shares its pattern of connections with the habenula, including the input from the subhippocampal-thalamic nucleus, and it can be regarded as an accessory habenular nucleus.

The pineal organ of lampreys has a pattern of projections different from the parapineal organ; it projects predominantly to subepithalamic sites within the diencephalon and to the midbrain—the optic tectum, posterior tubercle region of the tegmentum, reticular formation, and oculomotor nucleus.

In cartilaginous fishes, the epiphysis comprises a single outgrowth—the pineal organ. The pineal has rather widespread

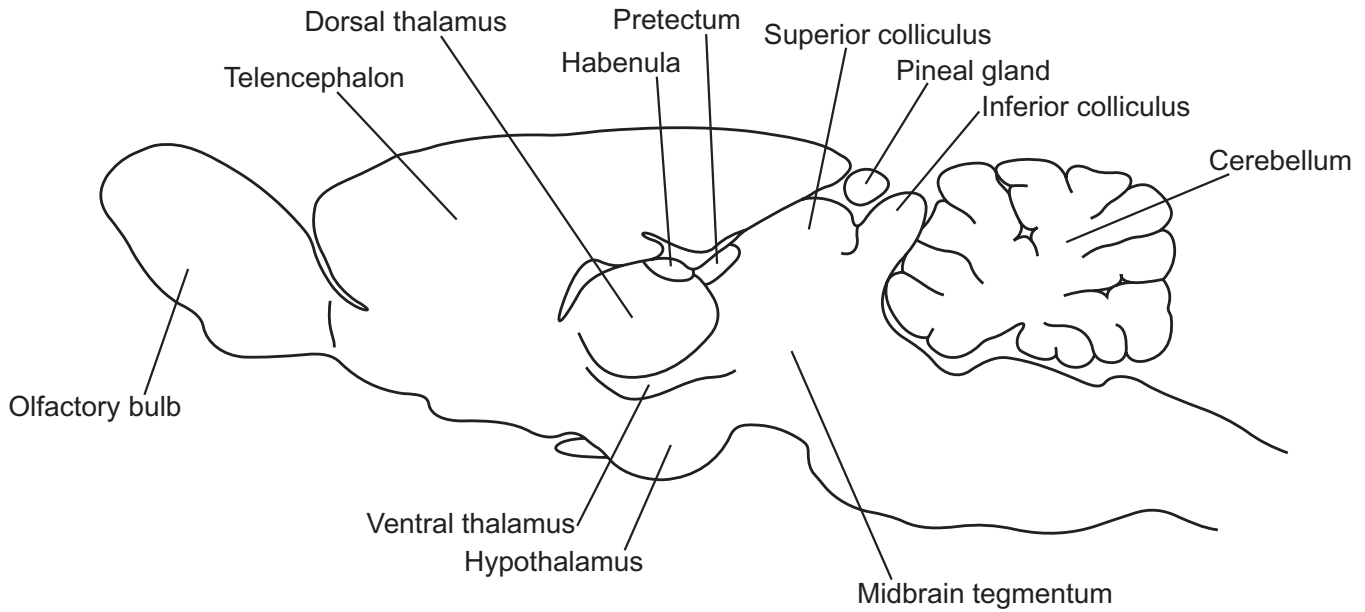


FIGURE 21-1. Drawing of a parasagittal section through the brain of a rat (*Rattus norvegicus*) showing the location of the pineal gland and the habenula. Adapted from Pellegrino et al. (1979) and used with kind permission of Springer Science and Business Media.

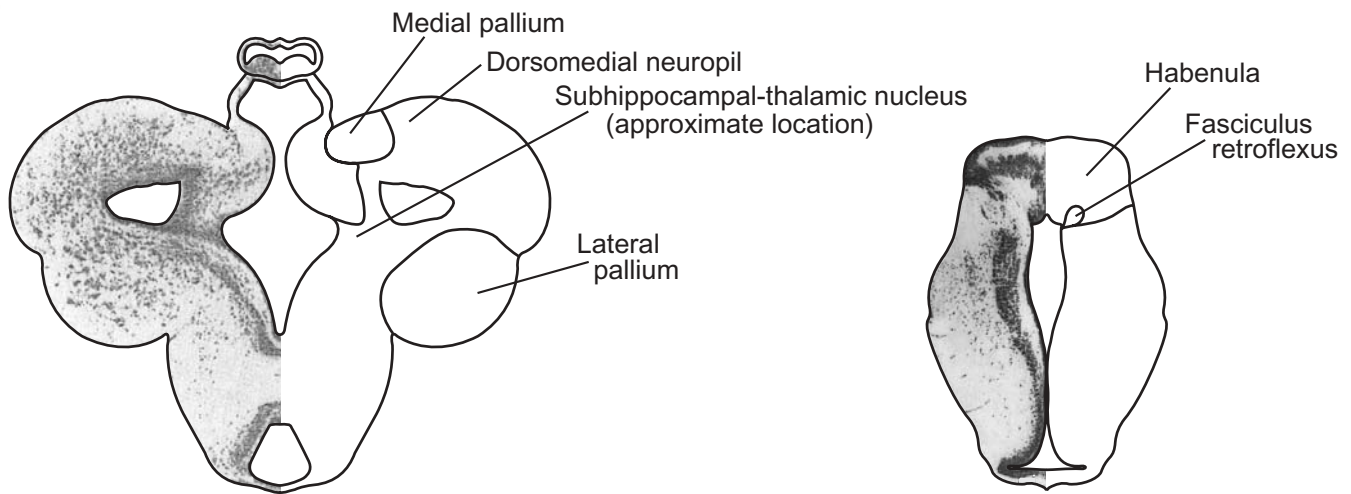


FIGURE 21-2. Transverse hemisections with mirror-image drawings through the telencephalon (left) and diencephalon of a lamprey (*Lampetra fluviatilis*). Note that the mirror-image drawing on the right does not demonstrate the left-to-right sided asymmetry of the habenula, the larger, left one of which is shown here. Telencephalon section adapted from Northcutt and Wicht (1997) and used with permission of S Karger AG, Basel. Diencephalon section adapted from Pombal and Puelles (1999) and use with permission of John Wiley & Sons.

projections. Among its targets are the dorsomedial part of the thalamus, pretectal area, posterior tuberculum, and the medial part of the midbrain tegmentum. The pineal organ receives reciprocal projections from these sites as well as light input to its photoreceptor cells. An interesting feature of the pineal projections to the midbrain is that their target nucleus contains gonadotropin-releasing hormone (GnRH)-positive neurons, which are thought to give rise to widespread projections. Thus, this system appears

to provide a direct route for pineal mediation of brain activity based on the light-dark cycle. Since a similarly located GnRH-positive cell group is also present in the tegmentum and is innervated by pineal fibers in other anamniotes, including ray-finned fishes and amphibians, a pineal-GnRH projection system may be a generalized feature of these taxa.

Only a single epiphyseal outgrowth is present in most ray-finned fishes, and, as in cartilaginous fishes, pineal projections

are rather widespread. Pineal fibers project to the habenular nuclei and to areas within the dorsal and ventral thalamus, periventricular part of the hypothalamus, and pretectum, as well as to the GnRH-positive cell group of the tegmentum. Minor projections also reach the interpeduncular nucleus and the optic tectum. A trout has been found to have both the pineal organ and a small parapineal organ. The latter projects mainly to the left habenula, with a few fibers also projecting to the habenular nucleus on the right side. The parapineal organ in the trout does not receive any reciprocal projections from the habenula, however, nor apparently from any other cell group in the brain.

All amphibians have a pineal gland, and frogs additionally have a more rostral part of the epiphysis called the frontal organ, which is similar to the parietal eye of lizards. Most lizards and the tuatara *Sphenodon* have a parietal eye (see Chapter 2), with a pigmented retina, in addition to the pineal gland. Turtles and snakes have only a pineal gland, and adult crocodiles lack an epiphysis. Pineal and parapineal outgrowths are present in bird embryos, but only the glandular pineal persists in adults. A single epiphyseal outgrowth, the pineal gland, is present in most mammals, including monotremes.

In amphibians, projections of the pineal organ to sites in the diencephalon and midbrain are similar to those in lampreys and jawed fishes, and the photoreceptors of this organ mediate a variety of functions. The pineal organ of newts recently has been found to participate in the animals' orientation to the magnetic compass by a response to long-wavelength light. In tadpoles, swimming responses to dim light may involve a pathway from the pineal organ to a group of neurons in the ventral mesencephalon, which in turn project to motor centers in the spinal cord. A second outgrowth of the epiphysis, the frontal organ, is present in amphibians; it projects to the left habenula as well as to other brainstem sites. However, unlike the parapineal organ of lampreys and some fishes, the frontal organ is an outgrowth of the caudal part of the epiphysis, and most of its connections are similar to those of the pineal rather than to those of the habenula.

Pineal projections, long thought to be absent in mammals, are present although relatively restricted. They terminate in the medial habenular nucleus and the pretectum in the region of the posterior commissure. Cells in the medial and lateral habenular nuclei project to the pineal organ, as do ependymal cells that line the pineal and parapineal recesses and are in contact with cerebrospinal fluid. A sympathetic input to the pineal is also present.

In reptiles, the pineal organ is known to project to parts of the diencephalon and mesencephalon, but the details of this projection remain to be worked out. The parietal eye gives rise to fibers that pass through and may terminate in the habenula. Parietal efferent fibers also project to the dorsolateral part of the dorsal thalamus, pretectum, periventricular part of the hypothalamus, preoptic area, and nucleus of the diagonal band in the septal area of the telencephalon. Additionally, a sparse epiphysopetal projection from scattered neurons in the periventricular part of the hypothalamus to the parietal eye is present.

Pineal projections are relatively restricted in birds. Avian pineal cells have irregular membrane segments that are similar to the outer segments of retinal photoreceptor cells that

contain opsin, the protein that combines with vitamin A to form the photosensitive pigment rhodopsin (visual purple). Efferent fibers from the pineal project to the medial and lateral habenular nuclei and to the periventricular part of the hypothalamus. Epiphyseal projections do not reach parts of the dorsal or ventral thalamus, pretectum, or mesencephalon, however. As in reptiles, epiphysopetal projections to the pineal are present and originate from cells in the habenular nuclei and in the periventricular part of the hypothalamus. The pineal in birds is also known to receive a sympathetic nervous innervation from neurons in the superior cervical ganglion.

The role of the epiphysis in the regulation of circadian and other biological rhythms is well established, but the anatomical substrate for its activity has not been fully clarified. Photoreceptor cells are present within the epiphysis in most vertebrates. Cells within the pineal organ secrete melatonin and other regulatory hormones directly into the blood so that biological rhythms can be regulated by neuroendocrine control. The epiphysis also regulates biological rhythms via a number of connections of the epiphyseal cranial nerve.

The majority of projections from the epiphysis overlap regions to which the retina projects, indicating a complementary role for some retinal and some epiphyseal inputs in regulating circadian rhythms. The epiphysis may also be involved in behavioral thermoregulation, such as some reptiles use to maintain body temperature during the daylight period. The epiphyseal projections to parts of the thalamus and hypothalamus, particularly the periventricular hypothalamus and preoptic area, are to areas containing estradiol-concentrating neurons. These epiphyseal projections may affect gonadotropin secretion and mating behavior, which is seasonal and thus influenced by day-night periodicity. Additionally, the GnRH-positive projection system of amniotes, which receives pineal input, may affect these behaviors. In birds, electrophysiological responses of pineal cells to artificially applied magnetic fields have been demonstrated, so a role for the pineal in the regulation and guidance of seasonal migrations is a possibility. Likewise, in newts, the pineal is involved in magnetic compass orientation.

Among jawed vertebrates, the presence of neurons in the brain—particularly the system via the suprachiasmatic nucleus—that project epiphysopetally appears to be an apomorphic feature for amniotes. These neurons may be part of a multisynaptic pathway that relays information about the day-night cycle from the retina to the epiphysis. The retina projects to a nucleus in the preoptic area called the suprachiasmatic nucleus. Bilateral lesions of the suprachiasmatic nucleus result in disruptions of cyclic hormone secretions in the pineal organ, the circadian rhythms, and the estrous cycle.

HABENULA

One of the most striking morphological features of the habenula is that in many vertebrates it is markedly asymmetric in size on one side of the brain versus the other. The biological significance of this variation, if any, is unknown. In all vertebrates, the major afferent tract to the habenula from the telencephalon—particularly the septal nuclei—and other sources is the **stria medullaris** (shown in a lizard in

Fig. 21-6). The major efferent tract is the **fasciculus retroflexus** (or **habenulo-interpeduncular tract**) and is universally present in all fishes and in tetrapods. It is a discrete fiber bundle with a round shape in transverse section that courses through the dorsomedial parts of the dorsal thalamus and pretectum and thence to the interpeduncular nucleus in the brainstem. The position of the fasciculus retroflexus (FR) in the pretectal region is shown in a number of the figures in Chapter 20.

The habenular complex is well developed and prominent in lampreys (Fig. 21-2), hagfishes (Fig. 21-3), and cartilaginous and ray-finned fishes (Fig. 21-4). In lampreys, the habenula receives afferent projections from a region in the telencephalon, which is called the lobus subhippocampalis. Several sites in the telencephalon project to the habenula in cartilaginous fishes, including the ventromedially lying septal nuclei. Neurons in the caudal part of the septal region also give rise to direct projections to the interpeduncular nucleus.

In goldfish, inputs to the habenula from several areas, including the entopeduncular nucleus and the dorsal nucleus of area ventralis, Vd, in the telencephalon, have been found. Vd currently is considered to be homologous to all or part of the striatum of amniotes; its projection to the habenula is consistent with this interpretation but not diagnostic, since the habenula in tetrapods receives inputs from both limbic (septal) and striatopallidal sources. In a trout, habenular afferents have been found to arise from several sites—the entopeduncular nucleus, a cell group in the hypothalamus-posterior tubercular region called the tuberculohabenular nucleus, and the preoptic nucleus. The epiphyseal components—the pineal and parapineal organs—also project to the habenula.

In amphibians, the habenular complex is known to receive limbic afferents from the septal area and bed nucleus of the hippocampal commissure and striatal afferents from the

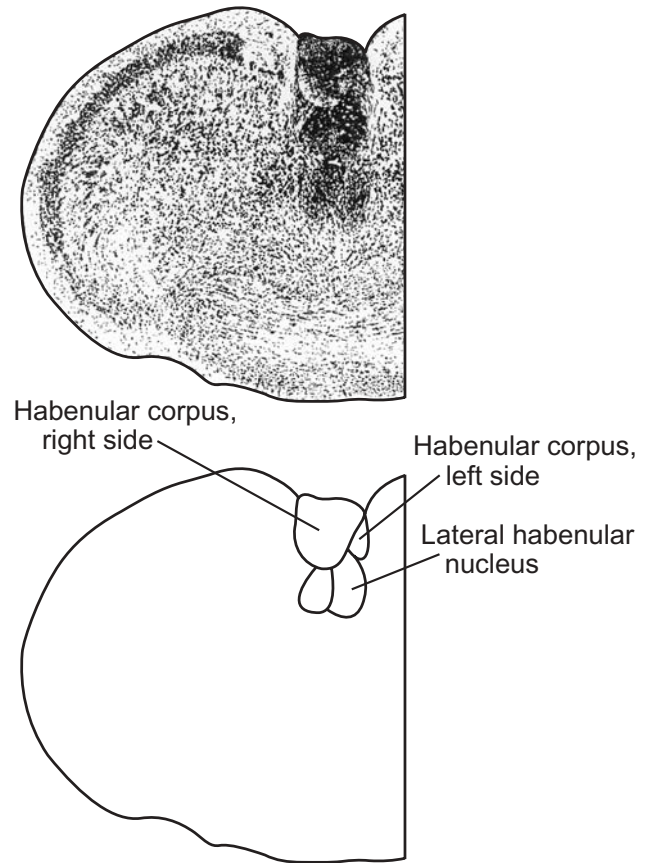


FIGURE 21-3. Transverse section with drawing through the habenula of a hagfish (*Eptatretus stouti*). Adapted from Wicht and Northcutt (1992) and used with permission of S Karger AG, Basel.

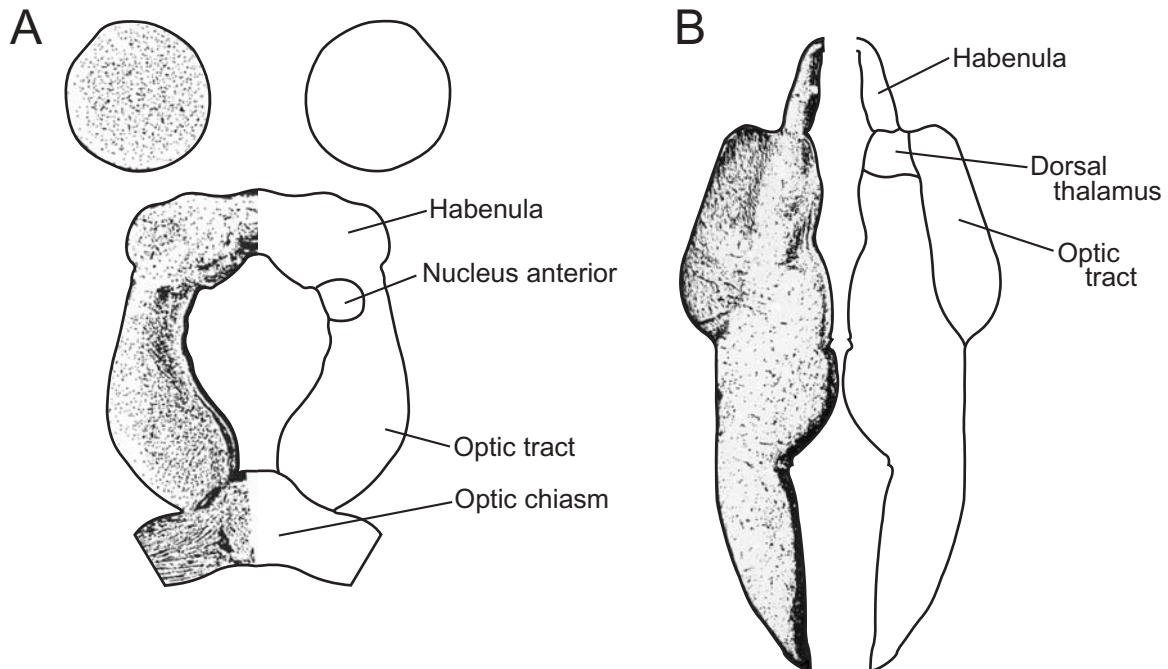


FIGURE 21-4. Transverse hemisections through the habenula of a squalomorph shark (*Squalus acanthias*), on the left, and the bowfin (*Amia calva*), on the right. Adapted from Northcutt (1979) and Butler and Northcutt (1992), respectively, and used with permission of Elsevier and S Karger AG, Basel, respectively.

entopeduncular nucleus (the homologue of the internal segment of the globus pallidus of primates). Input to the habenula also arises from part of the hypothalamus. The habenula projects to sites in the brainstem, including the interpeduncular nucleus.

The multiple connections of the epithalamus are most thoroughly worked out in mammals. In mammals, the epithalamus includes the habenular nuclei and two additional nuclei called the **anterior and posterior paraventricular nuclei**. The latter two nuclei are reciprocally connected with structures that are part of or related to the limbic system: the amygdala, the lateral hypothalamus, and the hippocampal formation (Fig. 21-5).

The habenula in mammals contains medial and lateral habenular nuclei. The medial habenular nucleus is interconnected with the limbic system (Fig. 21-5). It receives

inputs from the septofimbrial and triangular nuclei in the caudal part of the septal region, the nucleus of the diagonal band in the medial part of the septal region, and the lateral preoptic and lateral hypothalamic areas. The medial habenular nucleus projects to the interpeduncular nucleus via the fasciculus retroflexus. The interpeduncular nucleus projects to the hippocampal formation, which in turn projects back to the septal nuclei, thus forming a feedback loop for the integration of limbic system information. In addition, the interpeduncular nucleus projects to the tegmental reticular formation, which also receives input from the lateral habenular nucleus.

The lateral habenular nucleus—particularly its lateral part—receives inputs from diverse sources related to both the striatum and the limbic system (Fig. 21-5)—particularly the entopeduncular nucleus (i.e., the internal segment of the globus pallidus), the ventral tegmental area, the lateral

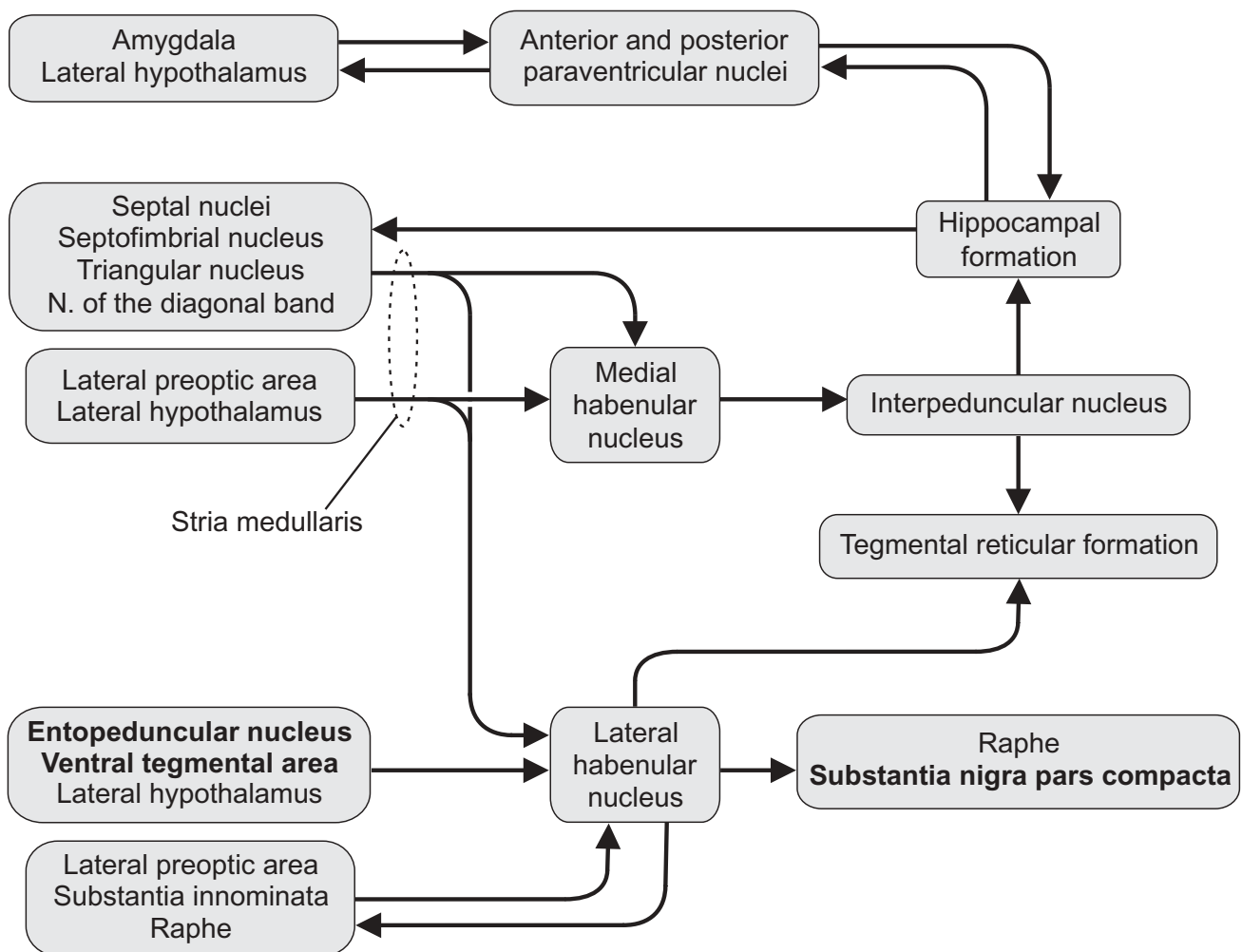


FIGURE 21-5. Diagram of connections of the habenular nuclei in mammals. The connections of the anterior and posterior paraventricular nuclei are shown at the top. The medial habenular nucleus is shown in the middle of the figure. Its afferent sources are limbic structures, particularly the septal nuclei, which project to it via the stria medullaris. The components of this tract are indicated by the oval ring. The medial habenular nucleus participates in limbic circuitry via the interpeduncular nucleus. The lateral habenular nucleus and its connections are shown at the bottom. In addition to receiving projections from limbic structures via the stria medullaris, the lateral habenular nucleus also participates in motor-related circuitry, as indicated by the structures in boldface type.

hypothalamus, the substantia innominata, the lateral preoptic area, and the midbrain raphe. The main efferent projections of the lateral habenular nucleus are to motor-related targets, including the tegmental reticular formation and the pars compacta of the substantia nigra. The lateral habenular nucleus also projects to the raphe. Thus, the anterior and posterior paraventricular nuclei and the medial habenular nucleus are predominantly interconnected with the limbic system. The lateral habenular nucleus receives similar limbic system inputs but

also receives motor-related inputs from the striatopallidal system and its related components.

In reptiles (Fig. 21-6) and birds, only limited information is available on habenular connections. Inputs to the habenula from both striatal and limbic (septal) sources have been found, as well as from parts of the preoptic area and hypothalamus. The habenula projects via the fasciculus retroflexus to the interpeduncular nucleus and presumably to other sites in the brainstem as well.

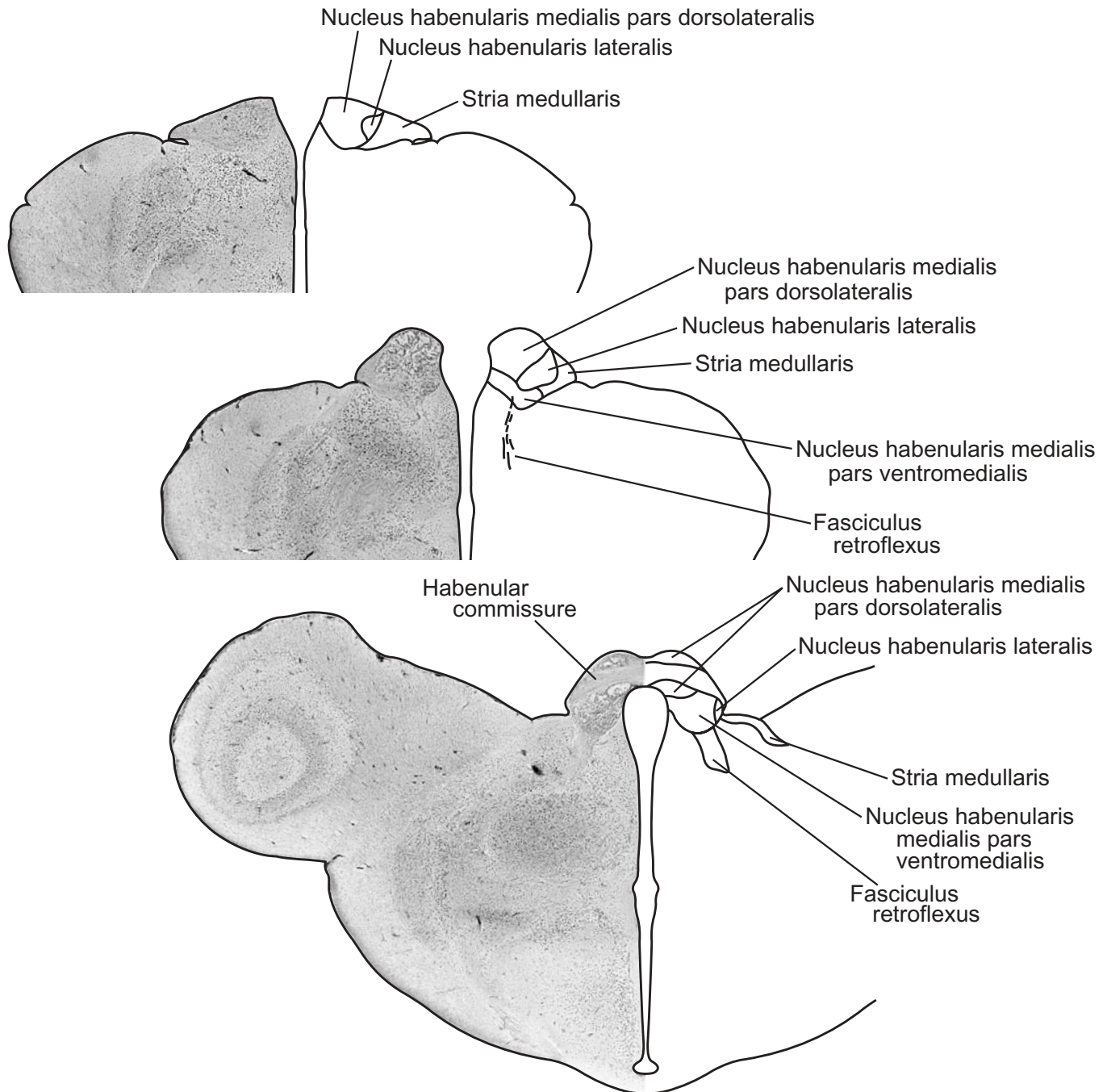


FIGURE 21-6. Transverse hemisections with mirror-image drawings through the habenular region of a lizard (*Iguana iguana*). The most rostral section is at the top left. Adapted from Butler and Northcutt (1973).

BOX 21-I. A Strange Nucleus in Some Ray-Finned Fishes

Some ray-finned fishes have a nucleus that may be an additional part of the epithalamus and perhaps some sort of supernumerary habenula. This nucleus is named **nucleus rostrrolateralis** due to its rostral and lateral position within the diencephalon. No known homologue of this nucleus is present in any other vertebrate group.

Unlike other parts of the epithalamus, nucleus rostrrolateralis receives visual inputs from the retina and the optic

tectum, and, in the zebrafish, it has been found to give rise to a minor projection to the ventral part of the telencephalon. Like the habenula, it sends some of its efferent axons caudally via the fasciculus retroflexus to the interpeduncular nucleus. Nucleus rostrrolateralis is of particular interest due to its extremely sporadic phylogenetic distribution. It occurs in several clusters of closely related taxa that are only very distantly related to each other, and it is absent in many taxa of intermediate phylogenetic position. Where present, it exhibits multiple similarities, not only of connections but also of position, cytoarchitecture, and histochemistry. It is thus probably a product of the same set of genes, inherited from the common ancestor of at least neopterygian fishes (gars, halecomorphs, and teleosts—see Chapter 4) but is only expressed phenotypically in a very few and far-flung taxa. As noted in Chapter 1, this nucleus appears to be an example of syngeny, or generative homology, as also noted above for the parapineal organ/parietal eye structure. Syngeny comprises most cases of phylogenetic homology, where the character is consistently expressed in the phenotype across the taxon, and also encompasses reversals of expression along a lineage and cases of far-flung parallelism, such as nucleus rostrrolateralis.

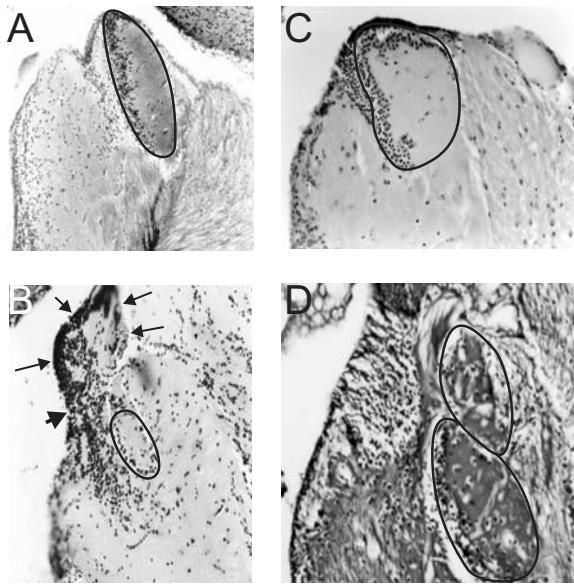


FIGURE 1. Transverse hemisections through the dorsal and lateral part of the diencephalon of four teleost fishes, the osteoglossomorph *Pantodon buchholzi* (A), the euteleost ostariophysan *Danio rerio* (B), and two euteleost acanthopterygians, *Gambusia affinis* (C) and *Anableps anableps* (D). The nucleus is outlined in black. In B, the smaller arrows point to the border of the habenula, with the larger arrow pointing to its ventromedial limit. In most cases, nucleus rostrrolateralis is quite large and salient, while in others, such as *Danio*, it is rather small. In the four-eyed fish *Anableps*, in which each eye is divided so that half remains out of the water looking into the air and the other half is submerged to view the water column, nucleus rostrrolateralis has two lobes on each side. Osteoglossomorphs (*Pantodon*) are phylogenetically basal to euteleosts, and within euteleosts, ostariophysans (*Danio*) are phylogenetically basal to acanthopterygians (*Gambusia* and *Anableps*). Nucleus rostrrolateralis also occurs in gars, which are phylogenetically basal to all teleosts. However, it is absent in many taxa that are phylogenetically intermediate to these various groups.

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EVOLUTIONARY PERSPECTIVE

The epithalamus itself and at least one of its components, the habenula, are present in all vertebrates and plesiomorphic for vertebrates. The habenula and its associated fiber tracts, particularly the fasciculus retroflexus, are very conservative features of vertebrate brains. Where sporadically present in some ray-finned fishes, nucleus rostrrolateralis may be an "extra" part of the habenula that uniquely receives visual input.

Variation occurs in the presence or absence of the components of the epiphysis. Fossil evidence reveals that an epiphysis was present in most ostracoderm and placoderm fishes and is thus plesiomorphic for vertebrates. An epiphysis has not been identified in hagfishes and may have been secondarily lost in this group. In lampreys, trout, and the coelacanth *Latimeria*, a rostral component of the epiphysis, the parapineal organ, is present and is connected with the left habenula. Likewise, the parietal eye of lizards and the tuatara may be parapineal derivatives. In lizards, the connections are known to be similar. This structure may have arisen and/or been lost several times independently across vertebrates; due to its similarities of development, photoreceptive neurons, and connections, it may be specified by the same patterning genes where present. Another component of the epiphysis, the frontal organ, is present in frogs. Unlike the parapineal organ, the frontal organ is a caudal epiphyseal component and has connections that are pineal in character.

The pineal component of the epiphysis is present in lampreys and all groups of jawed vertebrates, except crocodiles. The degree to which photoreceptor cells develop in one or both epiphyseal outgrowths is quite variable. In lampreys, both outgrowths contain photoreceptor cells, while in lizards and the tuatara, only the parietal eye is developed as a photoreceptive organ. This distribution suggests that the pineal component of the epiphysis is plesiomorphic for at least the common ancestral group of lampreys and jawed vertebrates and has been reduced and/or lost once in crocodiles. Efferent projections to the pineal are present in lampreys and amniotes, but the variability in the location of the central neurons suggests that these projections were evolved independently.

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22

Dorsal Thalamus

INTRODUCTION

The dorsal thalamus is a collection of nuclei within the diencephalon that relays ascending sensory, motor system-feedback, and related information to the telencephalon and is thus a crucial link between the external world and an animal's sensory experience of it. The dorsal thalamus is the key to the telencephalon in more ways than one; these two regions have extensive neuroanatomical connections and corresponding functional interactions, and the evolution of these two regions is similarly intertwined, particularly in amniotes. In this sense, the dorsal thalamus is a Rosetta stone for deciphering the history of forebrain evolution.

The way in which the organization of the dorsal thalamus of vertebrates is presented in this chapter represents a significant departure from previous treatments. The present weight of evidence indicates that many previously held ideas about the evolution of the dorsal thalamus are no longer plausible. The approach to dorsal thalamic organization taken in this chapter is based on a reinterpretation of forebrain evolution (see Butler, 1994a,b; 1995), which recognized two basic divisions of the dorsal thalamus—the **collothalamus** and the **lemnothalamus**. The collothalamic nuclei receive their predominant inputs via relays through the roof of the midbrain and tend to lie in the more caudal and ventral part of the dorsal thalamus. The lemnothalamic nuclei predominantly receive sensory, such as visual and/or somatosensory, inputs or other, sometimes diverse inputs, that predominantly reach these nuclei directly, without a relay through the midbrain roof. The lemnothalamic nuclei tend to lie in the more rostral and dorsal part of the dorsal thalamus.

We want to acknowledge here that this reinterpretation was independently arrived at by Margaret Martínez-de-la-Torre, Maria Caballero-Bleda, and Manoli Guillén. Working in the laboratory of Luis Puelles, they each also recognized the same basic organization within the dorsal thalamus as Butler did with her lemnothalamic and collothalamic divisions. Citations of their dissertations are included in the references at the end of this chapter. Since the identification of these divisions on hodological (connectional) grounds, additional hodological findings as well as molecular data have been obtained that support them. A number of recent references on various developmental aspects of the diencephalon are therefore listed as well.

Before the distinction between collothalamus and lemnothalamus was recognized, the organization of the dorsal thalamus had been difficult to make sense of due to the magnitude of variation in the number of its nuclear components across the range of vertebrate taxa. In most anamniote vertebrates, only three nuclei can be distinguished, and these nuclei lie in a periventricular position or are only slightly migrated away from the periventricular matrix (see Chapter 3). In contrast, the dorsal thalamus in amniotes is characterized by a multiplicity of distinct nuclei. This elaboration of the dorsal thalamus in amniotes contrasts with the elaboration of the pretectal and posterior tubercular regions in teleost fishes, as pointed out in Chapter 20. During development in some vertebrates, neurons migrate away from the region of the periventricular matrix where they are generated and form multiple, migrated nuclei in various parts of the brain. In the dorsal thalamus, this process occurs to a marked degree only in hagfishes and amniotes. It constitutes the single most important difference between the dorsal thalamus of amniotes and that of most

anamniotes. The central problem has been to identify where all of the nuclei that are present in the dorsal thalamus of adult amniotes come from—both in embryological and evolutionary terms.

In amniotes, two basic divisions of the dorsal thalamus can be recognized: (1) a rostral part, generally called nucleus anterior, that is in receipt of direct retinal projections and/or, in some cases, other projections, including lemniscal somatosensory projections; and (2) a more caudal part predominantly in receipt of inputs relayed to it from the midbrain roof. The rostral part is called the *lemnothalamus* in reference to the lemniscal nature of its inputs; that is, the sensory input pathways to it are direct, as opposed to being routed through an “extra” relay in the midbrain roof. The caudal part is called the *collothalamus* in reference to its predominant inputs being relayed through the midbrain roof—the colliculi, as its components are called in mammals. In amniotes, the *lemnothalamus* comprises a single nucleus, which projects bilaterally to the medial and dorsal pallia in the telencephalon, and the *collothalamus* comprises two or more nuclei, which predominantly project ipsilaterally to the striatum. In amniotes, a number of distinct nuclei are present in the dorsal thalamus. Several nuclei (or nuclear groups) receive their predominant input from the midbrain roof and comprise the *collothalamus*. A number of additional nuclei (or nuclear groups) are present, mostly in the rostral, dorsal region of the thalamus, which predominantly receive lemniscal sensory or other inputs and comprise the *lemnothalamus*.

The current interpretation of dorsal thalamic evolution (Fig. 22-1) encompasses the idea that the set of nuclei in each radiation of amniote vertebrates that does not receive its predominant input from the midbrain roof, and thus comprises the *lemnothalamus*, is homologous as a field to the nucleus anterior of anamniotes. In other words, the embryonic anlage that gives rise to nucleus anterior in anamniotes is hypothesized to be the same as that which gives rise to the rostral dorsal thalamic nuclei in amniotes. Embryologically, the territory of the developing *lemnothalamus* in mice is distinguished by the expression of a gene called *Math4a*.

The set of nuclei in the dorsal thalamus of amniotes that receives visual, auditory, somatosensory, and multisensory inputs from the midbrain roof likewise constitutes the *collothalamus*, as do the nuclei with similar inputs in the dorsal thalamus of anamniotes. Embryologically, this territory in mice is distinguished by neurons that are strongly positive for the calcium-binding protein calretinin. Although the possibility of parallelism or convergence cannot be dismissed in the elaboration of the dorsal thalamus of mammals and the elaboration of the dorsal thalamus in nonmammalian amniotes, the specified homologies as hypothesized here represent the most parsimonious interpretation of the known developmental and morphological similarities.

COLLOTHALAMIC AUDITORY SYSTEM

An ascending auditory pathway from the torus semicircularis (inferior colliculus) to a dorsal thalamic nucleus and thence to the telencephalon is a widespread feature of vertebrates. Among the *collothalamic* systems, we will discuss this

pathway first, because less controversy currently exists in comparisons of its components across vertebrate and particularly amniote taxa than for the visual and multisensory pathways.

Group I

In lampreys (Fig. 22-2), a dorsal thalamic region is present, but individual nuclei remain to be identified. In squalomorph sharks (Fig. 22-3) and nonteleost ray-finned fishes (Fig. 22-4), the dorsal thalamus contains three nuclei: **nucleus anterior**, which is *lemnothalamic*, and two *collothalamic* nuclei—the **dorsal posterior nucleus** and the **central posterior nucleus**. The dorsal thalamus of frogs (Fig. 22-5) has been divided into three rostral-to-caudal zones; slight migration, enlargement, and subdividing of the nuclei occurs, and the nomenclature is different from that in fishes in some respects. The middle zone contains the **central thalamic nucleus** (also called the **central posterior nucleus**), which is the relay nucleus for the auditory system.

Ascending projections of the torus semicircularis, which receives ascending auditory projections, have yet to be investigated in lampreys and squalomorph sharks. In nonteleost ray-finned fishes, the torus semicircularis projects to the central posterior nucleus (Fig. 22-4), and this nucleus projects to the striatum [called the dorsal nucleus of the ventral telencephalic area (Vd)]. The ascending auditory pathway varies in its complexity across amphibian taxa. In the bullfrog *Rana*, all three nuclei of the torus, the magnocellular, laminar, and principal nuclei, receive bidirectional projections from the hindbrain nuclei, whereas in the African clawed frog *Xenopus*, only the laminar nucleus receives such projections. Within the thalamus, several nuclei receive ascending axons from the toral nuclei with the predominant projections terminating in the **central and posterior thalamic nuclei** (Fig. 22-5). In *Rana*, the central nucleus projects predominantly to the striatum and slightly to the lateral part of the pallium. In *Xenopus*, no telencephalic projections from the thalamus have yet been reported.

Group IIA

Information on toral projections and the related ascending *collothalamic* pathways is lacking for hagfishes. Extended proliferation and migration of neurons in the dorsal thalamus occur in hagfishes, making comparisons with other vertebrates particularly challenging. Besides the possibly *lemnothalamic* nucleus anterior, three remaining nuclei—the **internal nucleus**, the **external nucleus**, and the **subhabenular nucleus**—have been identified (Fig. 22-6), but their homologies are uncertain.

In galeomorph sharks, skates, and rays (Fig. 22-7), forebrain auditory pathways also remain to be studied, but auditory evoked potentials have been recorded from a part of the dorsal pallium, called the central nucleus, in the telencephalon. In the dorsal thalamus of most teleost fishes (Fig. 22-8), migration of neurons does not occur to as extensive a degree as in hagfishes and Group II cartilaginous fishes, although the two more caudal nuclei—the dorsal posterior and central posterior nuclei—both have laterally extending parts. The torus semicircularis projects to the central posterior nucleus (Fig. 22-8), which in turn projects predominantly to the striatum.

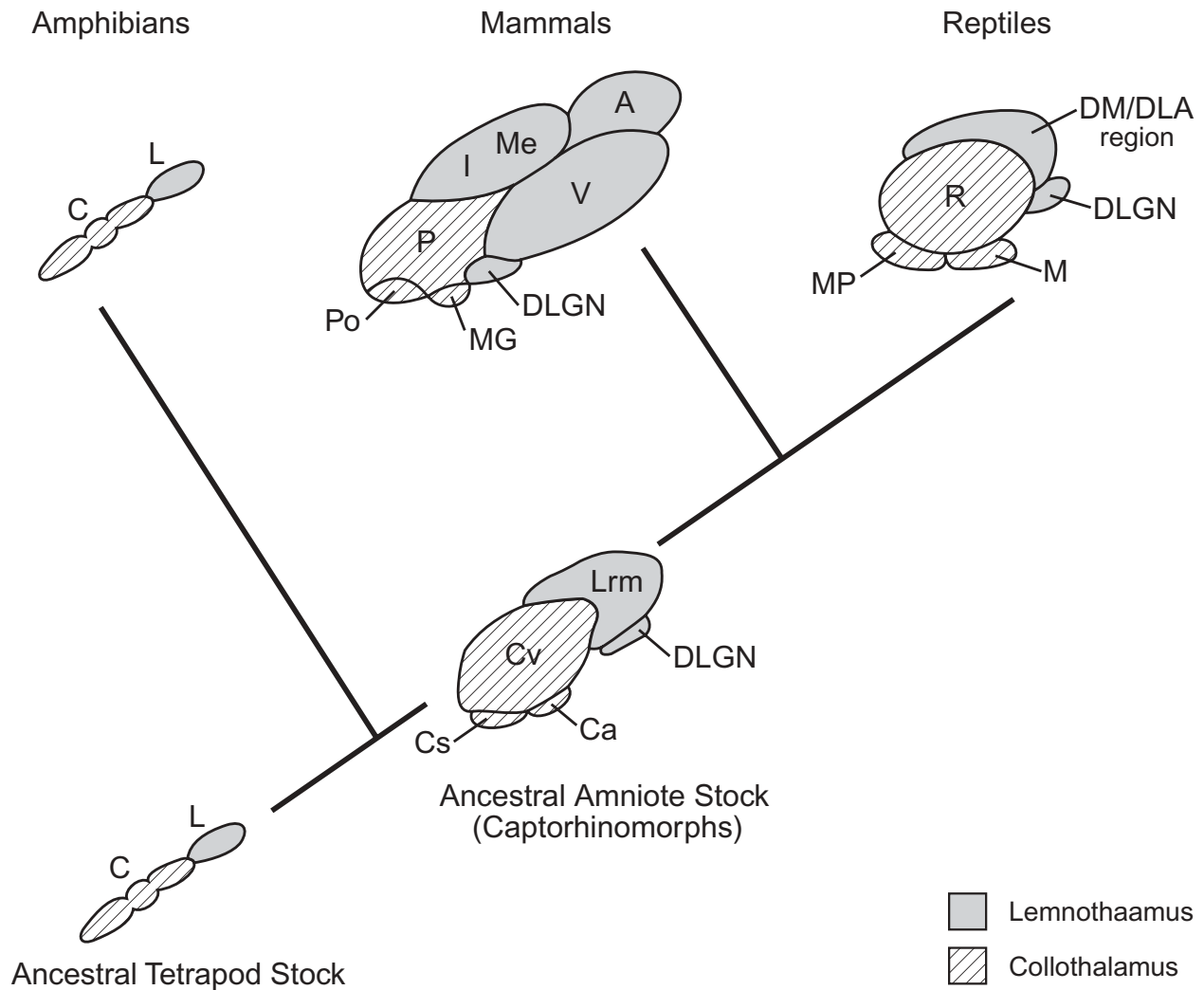


FIGURE 22-1. Summary of hypothesis (Butler, 1994a) of dorsal thalamic evolution in tetrapods in dendrogram form; oblique dorsolateral views of the whole dorsal thalamus, with rostral toward the upper right and medial toward the upper left. Lemnothalamic nuclei are indicated by shading and collothalamic nuclei by diagonal lines. A single lemnothalamic nucleus (nucleus anterior) and two or three caudal collothalamic nuclei (visual, auditory, and possibly somatosensory-multisensory) were present in ancestral tetrapods and are present in extant amphibians. In the ancestral amniote stock, both collothalamic and lemnothalamic divisions of the dorsal thalamus were elaborated; three collothalamic nuclei and at least two lemnothalamic nuclear areas were present. In the synapsid line that gave rise to extant mammals, a marked additional elaboration of the lemnothalamus occurred, resulting in a relatively larger expansion of this division of the dorsal thalamus than occurred in most nonmammalian amniotes. Among nonmammalian amniotes, birds (not represented in this figure) appear to have independently further elaborated their lemnothalamus. Abbreviations: A, anterior nuclear group; C, collothalamus; Ca, auditory collothalamic nucleus; Cs, somatosensory-multisensory collothalamic nucleus; Cv, visual collothalamic nucleus; DM/DLA region, region of nuclei dorsomedialis and dorsolateralis anterior; including somato-motor, olfactory relay, and other related cell groups; I, mediorostral intralaminar nuclear group; L, lemnothalamus; DLGN, dorsal lateral geniculate nucleus; Lrm, rostromedial part of the lemnothalamus; M, nucleus medialis (also called nucleus reunions pars compacta); Me, medial nuclear group; MG, medial geniculate body; MP, nucleus medialis posterior (also called the medialis complex); P, lateral posterior/pulvinar complex; Po, posterior and posterior intralaminar nuclear groups; R, nucleus rotundus; V, ventral nuclear group.

Additional ascending auditory axons terminate in the anterior hypothalamus and preoptic area in fishes and other vertebrate taxa as well.

One group of teleosts—the so-called *sonic fishes*—has a particularly well-developed auditory system. These fishes produce a variety of sounds that are used in courtship and other social behaviors. One such fish is the plainfin midshipman, (*Porichthys notatus*). The auditory thalamus of this animal is the **central posterior nucleus**, which projects to two telencephalic regions: the **dorsomedial nucleus of the telencephalon** and the **anterior ventral area of the telen-**

cephalon. The main ascending auditory pathway of the plainfin midshipman was diagrammed in Figure 12-5.

Group IIB

In reptiles, birds, and mammals, a greater number of distinct nuclei are present in the dorsal thalamus than in anamniotes. A number of these nuclei are shown in Figures 22-9, 22-10 and 22-11. Various names have been used for these nuclei, resulting in terminology that is cumbersome at best and that can be confusing and intimidating. Only selected terms are used here, as listed in Tables 22-1 and 22-2. Because Table 22-1 is based on primates, the reader should not expect to find every thalamic nucleus listed there in all orders of mammals. There is considerable variation among mammals in the number of nuclei and their subdivisions that can be distinguished within the dorsal thalamus.

In mammals, the inferior colliculus (homologue of the anamniote torus semicircularis) projects to the **medial geniculate body** [Fig. 22-9(F)]. The medial geniculate body has three major subdivisions—ventral, dorsal, and medial (or magnocellular). (The latter division is more appropriately grouped with the posterior nuclear group and posterior intralaminar nucleus, as discussed below.) The ventral division gives rise to the main pathway to primary auditory cortex, while the dorsal division projects to both primary and association auditory cortices. In addition to its cortical projections, the medial geniculate body also projects to two other telencephalic sites, the lateral nucleus of the amygdala within the pallium and the dorsal striatum within the subpallium.

In reptiles (Fig. 22-10), ascending auditory projections from the torus semicircularis terminate in **nucleus medialis** (which is alternatively called **nucleus reuniens pars compacta**). This nucleus, in turn, projects to a circumscribed part

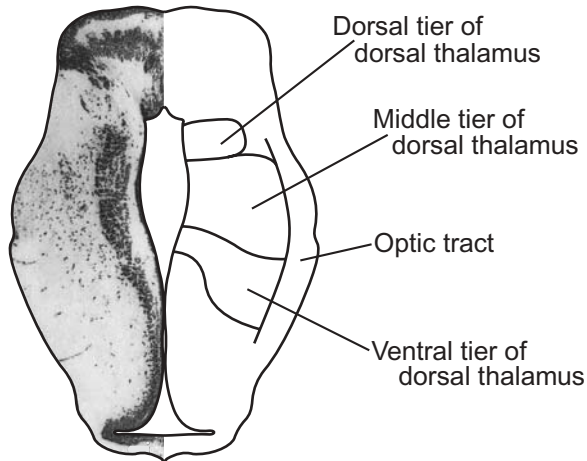


FIGURE 22-2. Transverse hemisection with mirror-image drawing through the diencephalon of a lamprey (*Lampetra fluviatilis*). Adapted from Pombal and Puelles (1999) and used with permission of John Wiley & Sons.

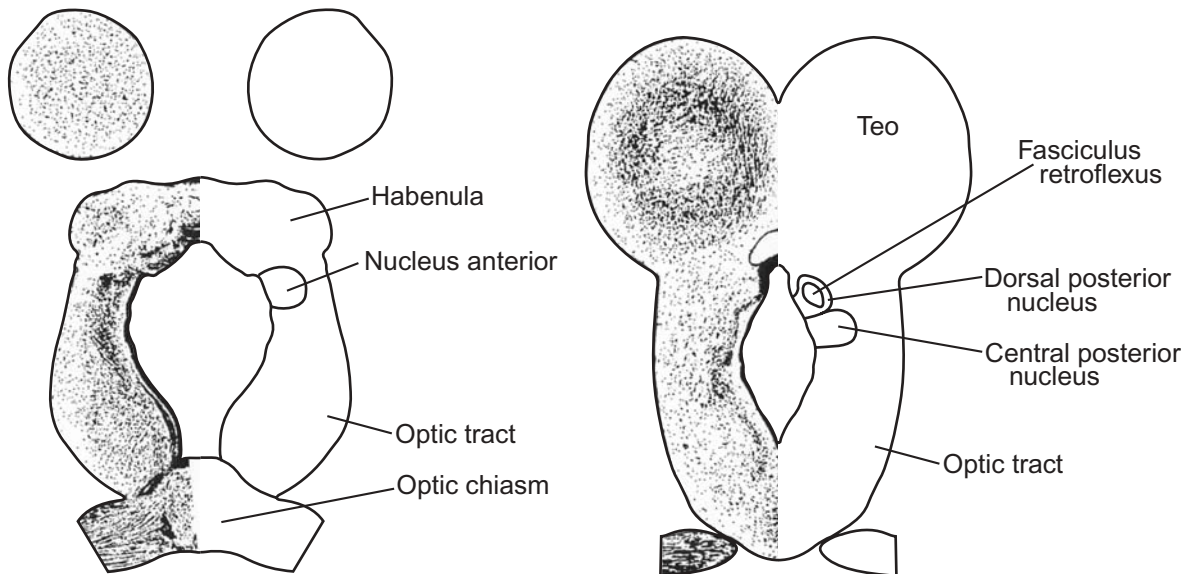


FIGURE 22-3. Transverse hemisections with mirror-image drawings through the diencephalon of a squalomorph shark (*Squalus acanthias*). The section on the left is more rostral. Adapted from Northcutt (1979) and used with permission of Elsevier.

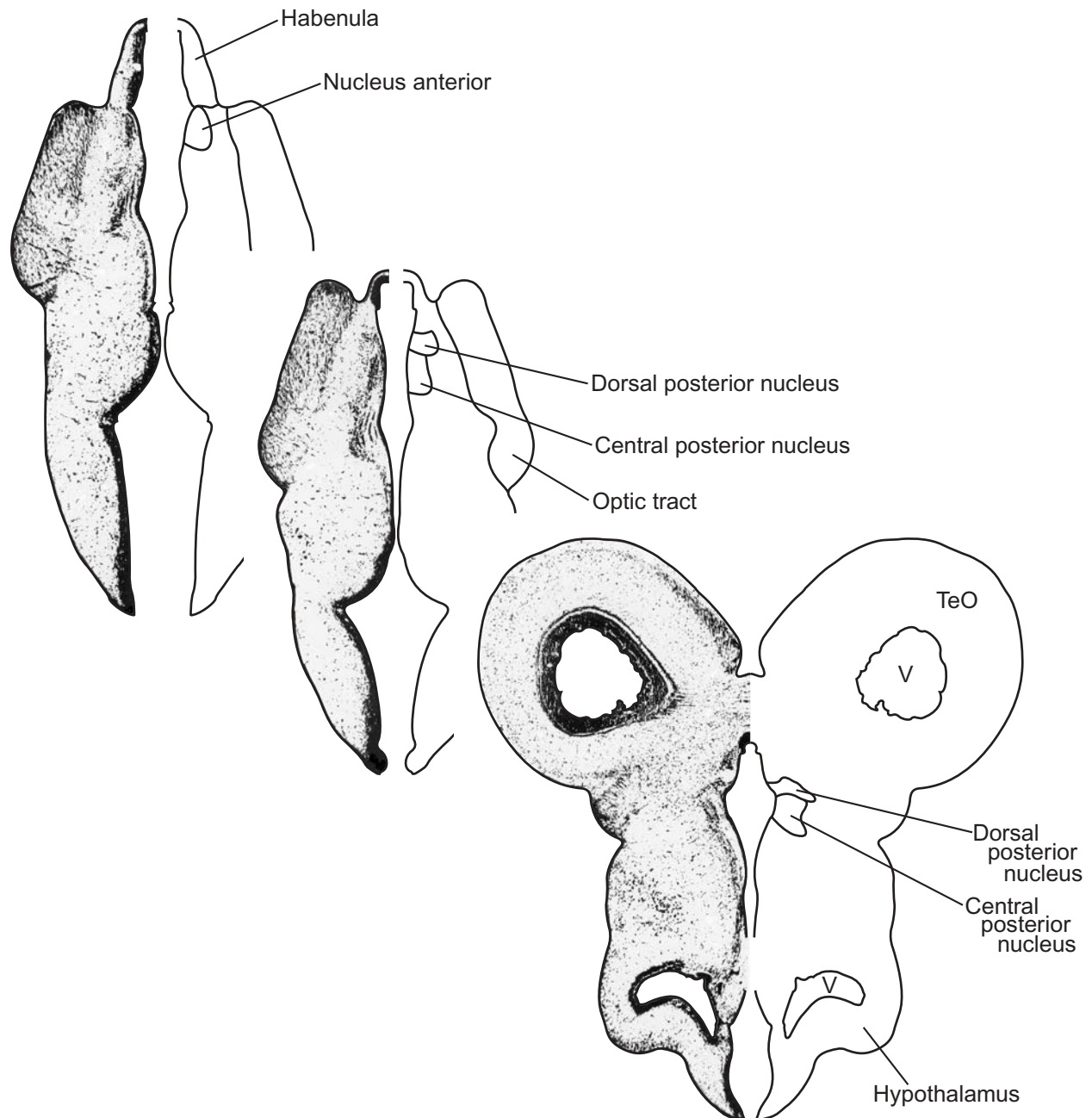


FIGURE 22-4. Transverse hemisections with mirror-image drawings through the diencephalon of a bowfin (*Amia calva*), with the most rostral section at the top left. Abbreviations: TeO, optic tectum; V, ventricle. Adapted from Butler and Northcutt (1992) and used with permission of S Karger AG, Basel.

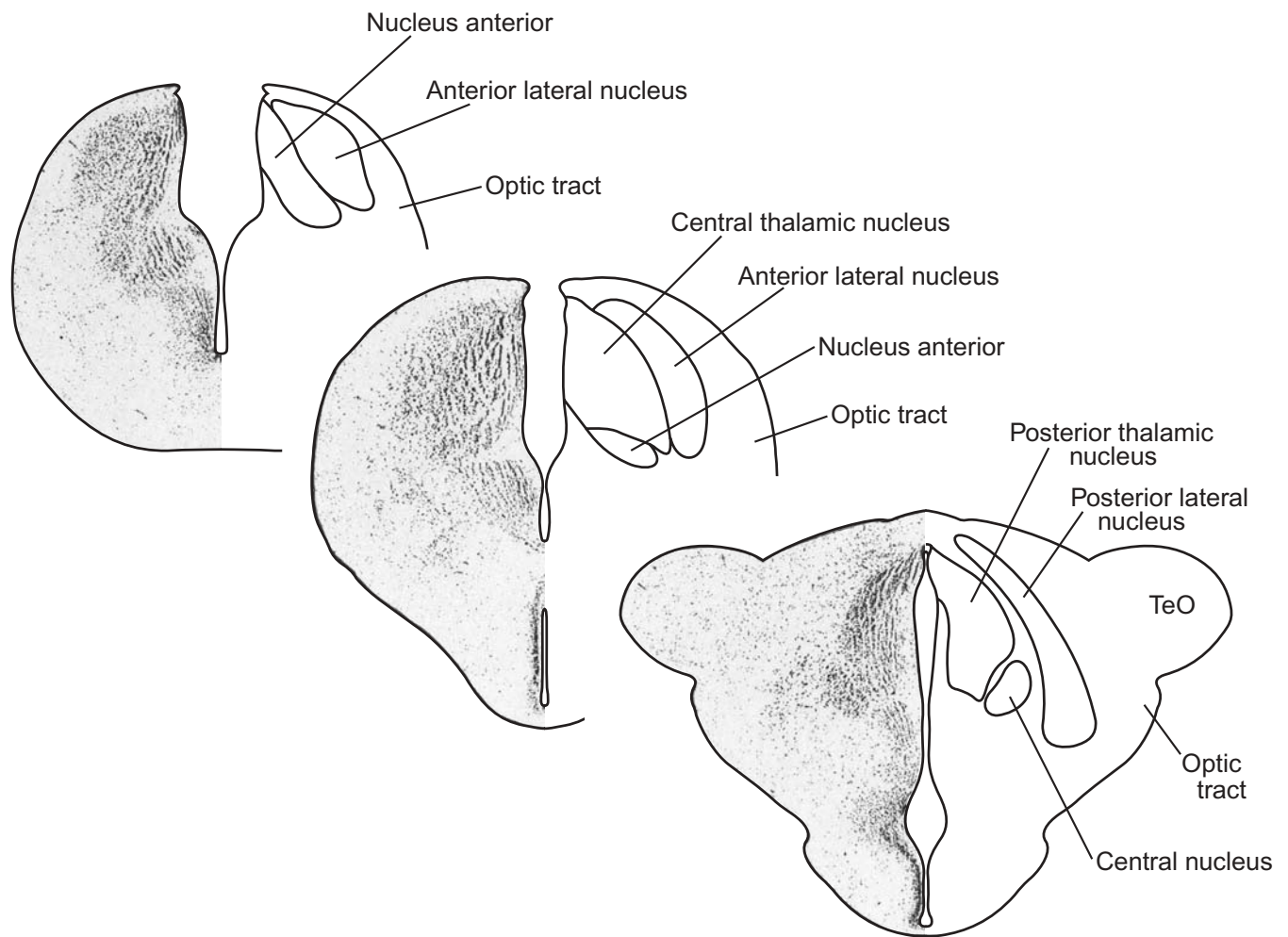


FIGURE 22-5. Transverse hemisections with mirror-image drawings through the diencephalon of a bullfrog (*Rana catesbeiana*). The top left section is most rostral. Abbreviation: TeO, optic tectum (rostral pole). Adapted from Neary and Northcutt (1983) and used with permission of John Wiley & Sons.

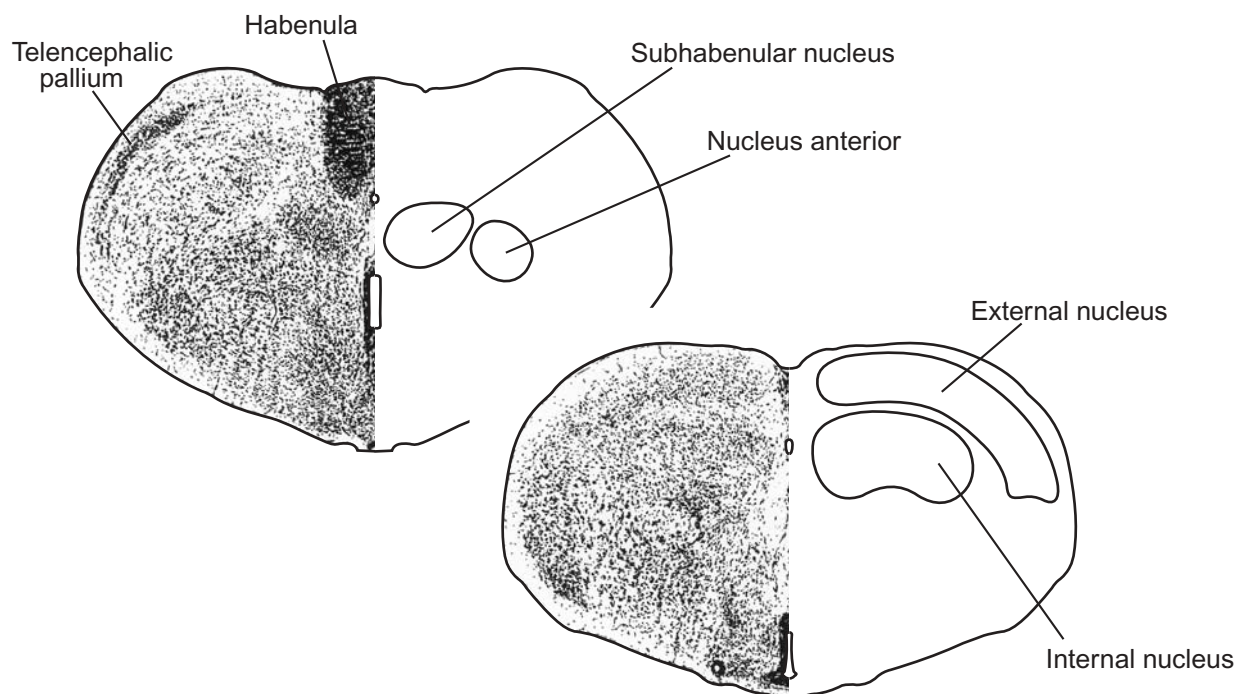


FIGURE 22-6. Transverse hemisections with mirror-image drawings through the diencephalon of a hagfish (*Eptatretus stouti*). The top section is more rostral. Adapted from Wicht and Northcutt (1992) and used with permission of S Karger AG, Basel.

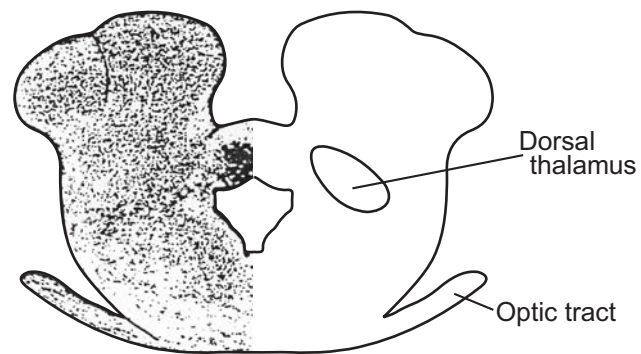


FIGURE 22-7. Transverse hemisection with mirror-image drawing through the diencephalon of a thornback skate (*Platyrhinoidis triseriata*). Adapted from Northcutt (1978).

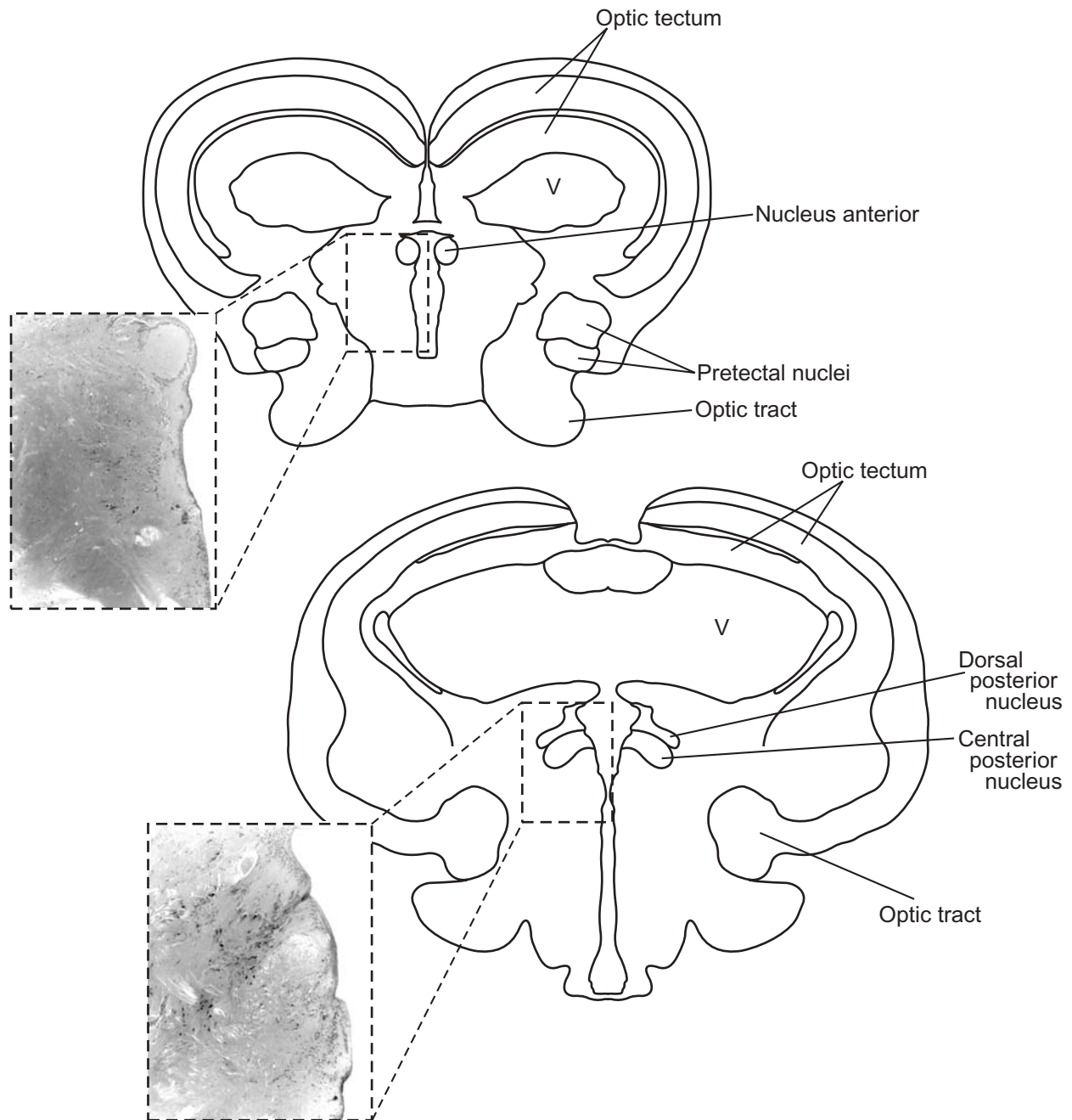


FIGURE 22-8. Drawings of transverse sections through the diencephalon of a teleost (*Clupea harengus*). The top section is more rostral. Boxes enclosed by dashed lines indicate areas shown as enlargements of Nissl photomicrographs. Adapted from Butler and Northcutt (1993).

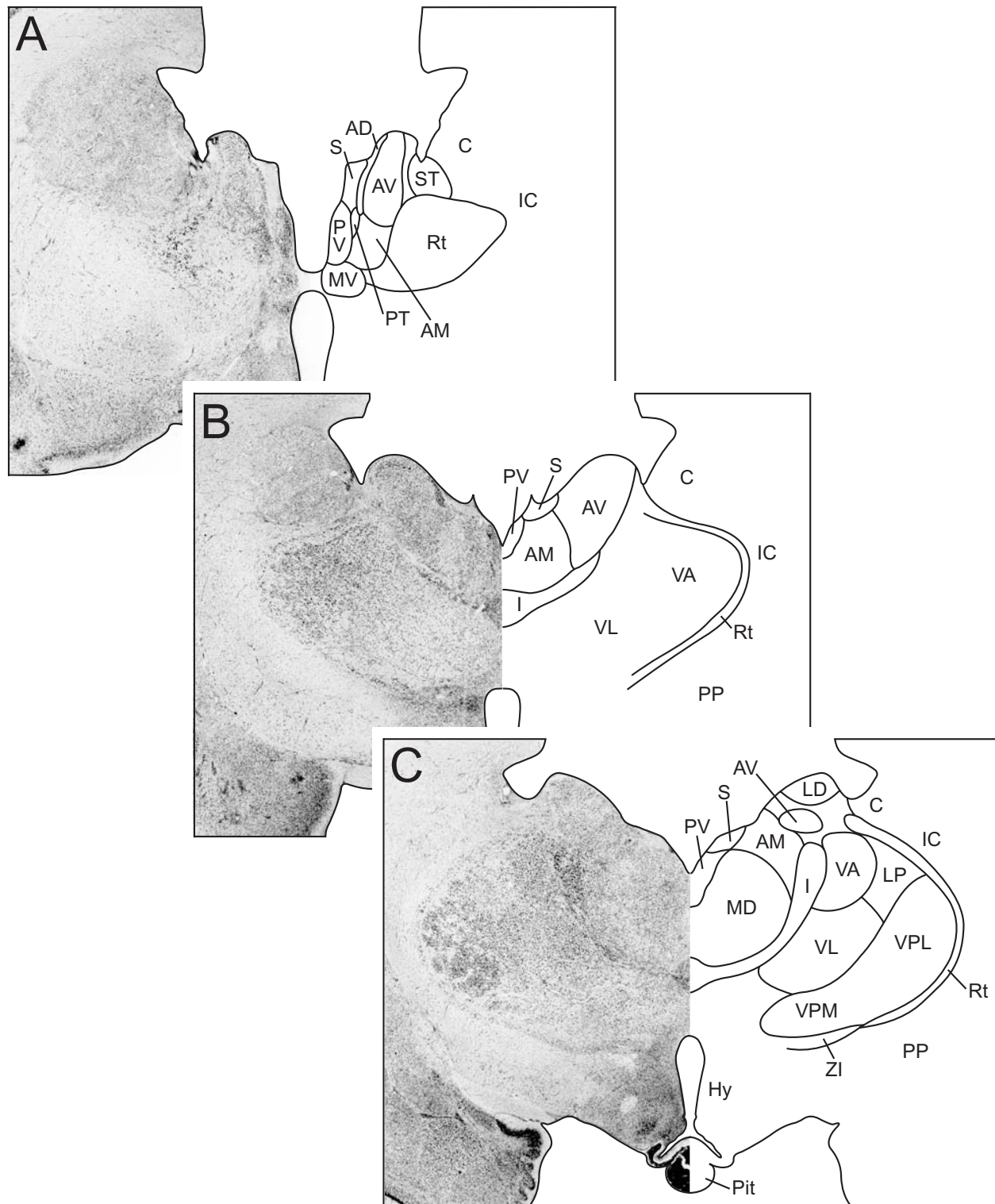


FIGURE 22-9. Transverse hemisections with mirror-image drawings through the diencephalon of a mammal (*Procyon lotor*) from rostral (A) to caudal (F). Abbreviations: AD, anterodorsal nucleus of the anterior nuclear group; AM, anteromedial nucleus of the anterior nuclear group; AV, anteroventral nucleus of the anterior nuclear group; C, caudate nucleus; CG, central gray; DLGN, dorsal lateral geniculate nucleus; Hy, hypothalamus; I, intralaminar nucleus; IC, internal capsule; LD, lateral dorsal nucleus, which is associated with the anterior nuclear group; LH, lateral habenula; LP, lateral posterior nucleus; MD, mediodorsal nucleus; MGN, medial geniculate nucleus; MH, medial habenula;

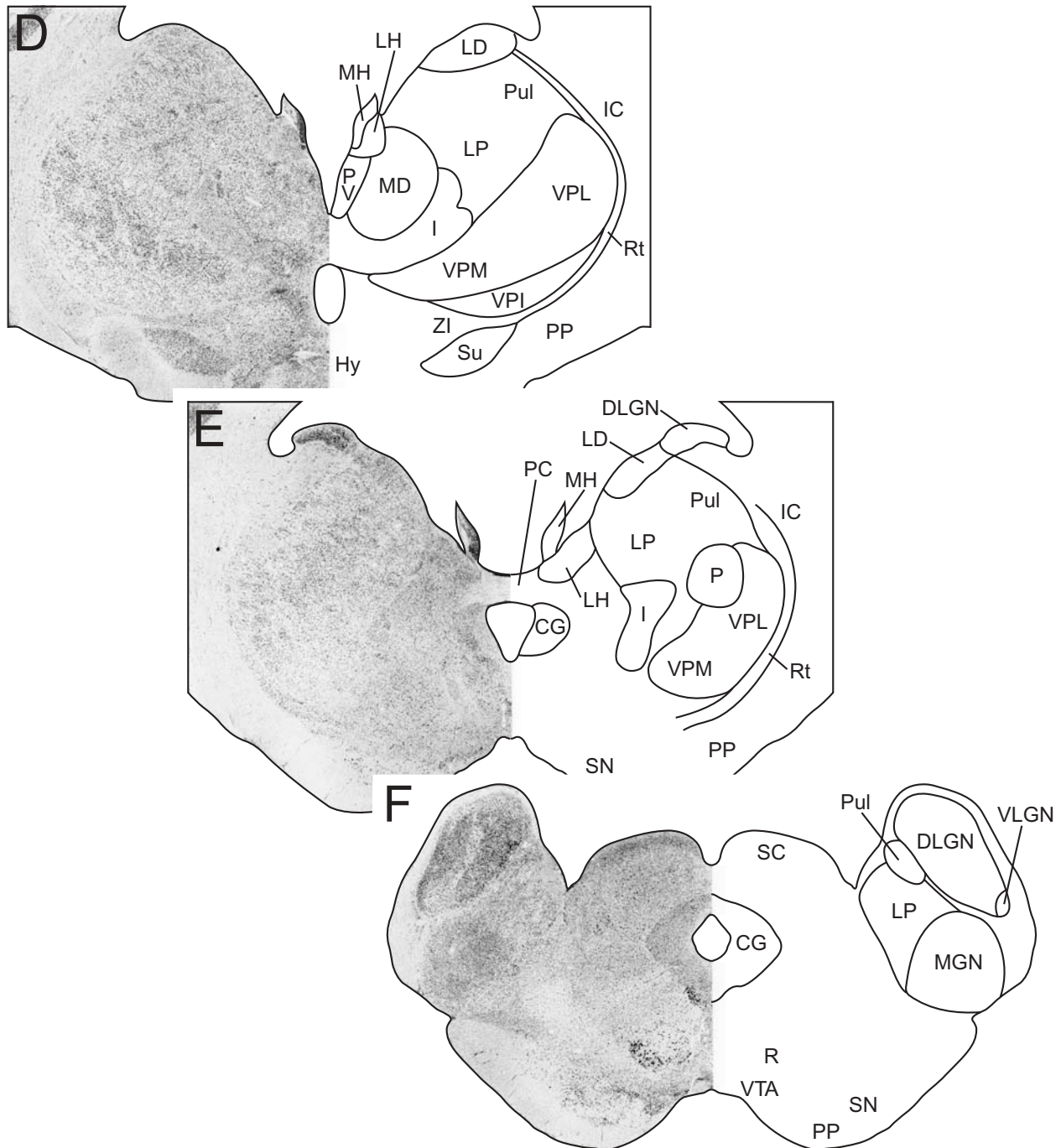


FIGURE 22-9. (Continued) MV, medioventral (reuniens) nucleus of the medial nuclear group; P, posterior nuclear group; PC, posterior commissure; Pit, pituitary; PP, pes pedunculi; PT, parataenial nucleus of the medial nuclear group; Pul, pulvinar; PV, paraventricular nuclear group of epithalamus; R, red nucleus; Rt, thalamic reticular nucleus (of the ventral thalamus); S, stria medullaris; SC, superior colliculus; SN, substantia nigra; ST, stria terminalis; Su, subthalamic nucleus; VA, ventral anterior nucleus of the ventral nuclear group; VL, ventral lateral complex of the ventral nuclear group; VLG, ventral lateral geniculate nucleus; VPI, ventral posterior inferior nucleus of the ventral nuclear group; VPL, ventral posterolateral nucleus of the ventral nuclear group; VPM, ventral posteromedial nucleus of the ventral nuclear group; VTA, ventral tegmental area; ZI, zona incerta. Photomicrographs and data on nuclear boundaries courtesy of Wally Welker.

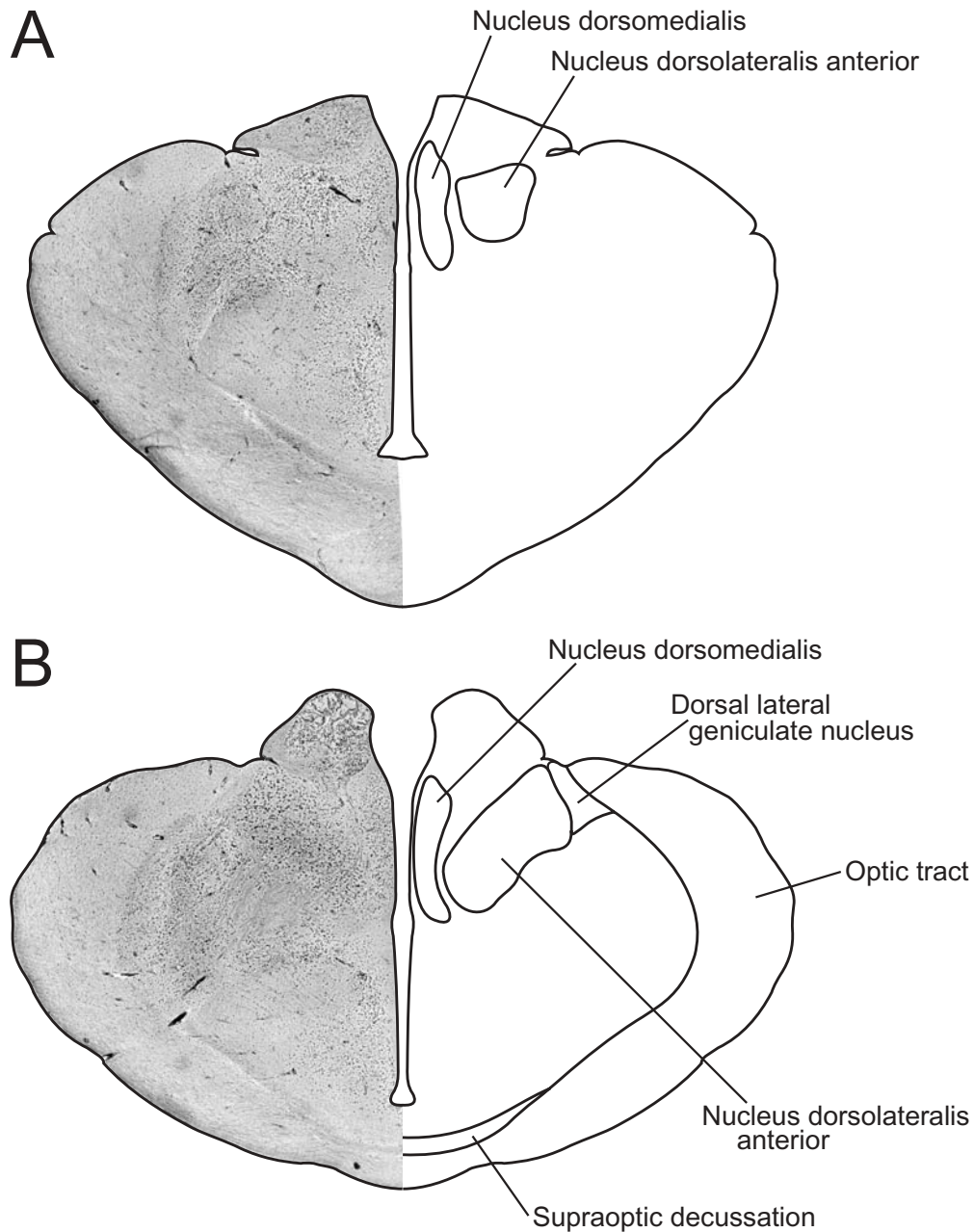


FIGURE 22-10. Transverse hemisections with mirror-image drawings through the diencephalon of a lizard (*Iguana iguana*). Section A is the most rostral. Abbreviation: TeO, optic tectum. Adapted from Butler and Northcutt (1973) with identification of the dorsal lateral geniculate nucleus based on Kenigfest et al. (1997).

of the dorsal ventricular ridge and to the striatum. In birds, the dorsal thalamic, auditory relay nucleus, **nucleus ovoidalis** (Fig. 22-11), projects to the auditory part of the dorsal ventricular ridge, called area *L pallii*, and to the striatum.

COLLOTHALAMIC VISUAL AND SOMATOSENSORY SYSTEMS

As we noted in Chapter 18, the optic tectum projects to multiple nuclei in the diencephalon. Within the dorsal thala-

mus, two or more visual tecto-recipient nuclei project to the telencephalon. The tectal input to one of these nuclei—the lemnothalamic nucleus anterior in anamniotes and the dorsal lateral geniculate nucleus in amniotes—is minor. The tectal visual input to the other nucleus or nuclei, which are collothalamoc, is substantial. Part of the midbrain roof—the deeper part of the optic tectum—also receives somatosensory inputs, and within the midbrain roof, some neurons integrate multi-modal information: somatosensory and auditory or somatosensory, auditory, and visual. Thus, the ascending pathways that carry this information to the

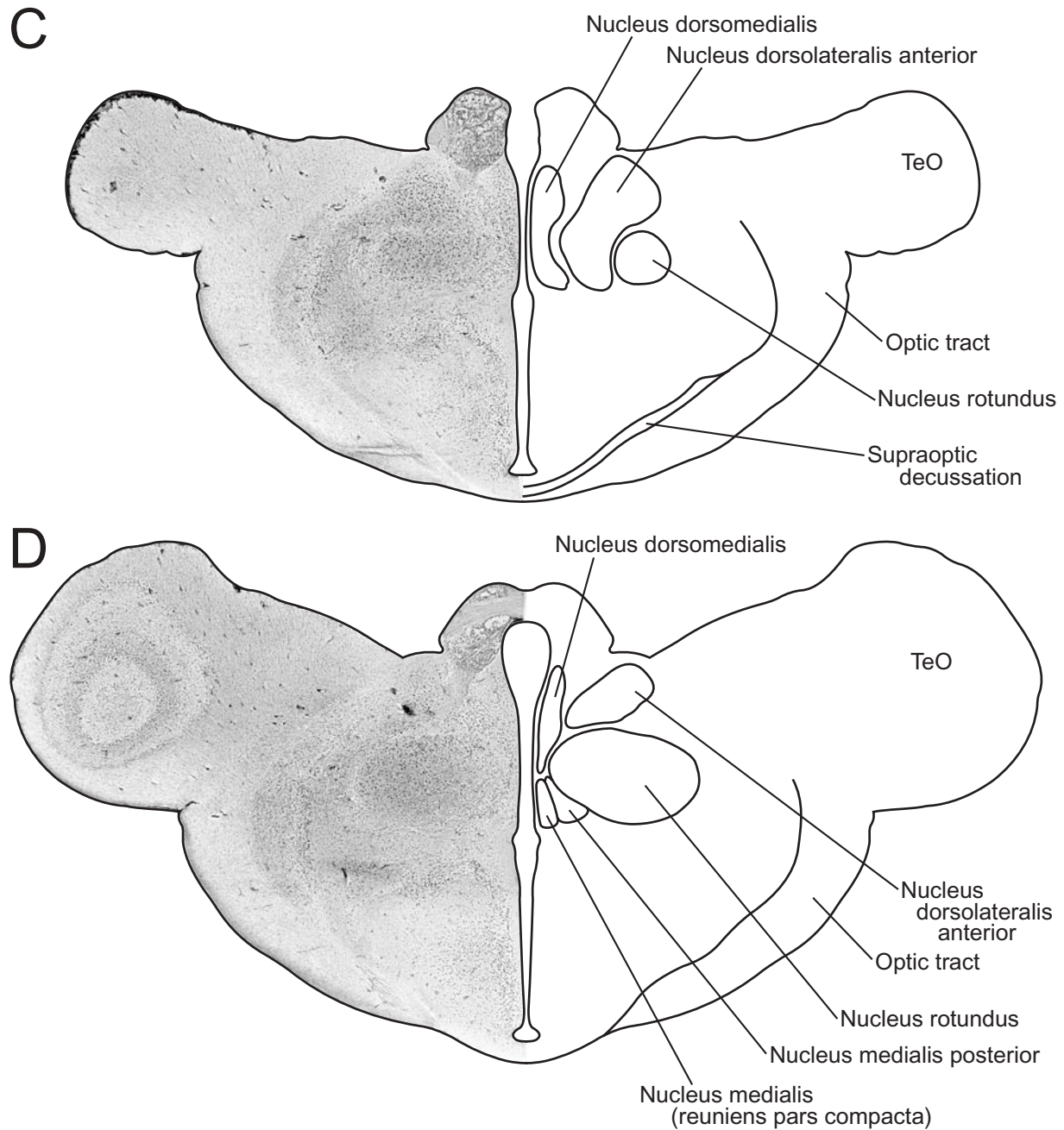


FIGURE 22-10. (Continued)

telencephalon via the dorsal thalamus are also considered in this section.

Group I

Studies have not yet been done in lampreys or squalomorph sharks to identify a particular set of neurons in receipt of tectal projections. In nonteleost ray-finned fishes, the optic tectum projects to the dorsal posterior nucleus (Fig. 22-4), which projects to the striatum in the telencephalon. Whether

this pathway is topographically organized has not been determined.

Two nuclei in the dorsal thalamus of frogs (Fig. 22-5)—the **anterior lateral nucleus** and the **posterior lateral nucleus**—receive most of the optic tectal projections. These projections are topographic only to the dorsal part of the posterior lateral nucleus, which does not project to the telencephalon. The anterior lateral nucleus receives nontopographic tectal input. It projects predominantly to the striatum and, to a minor extent, to the lateral pallium. Whether only the

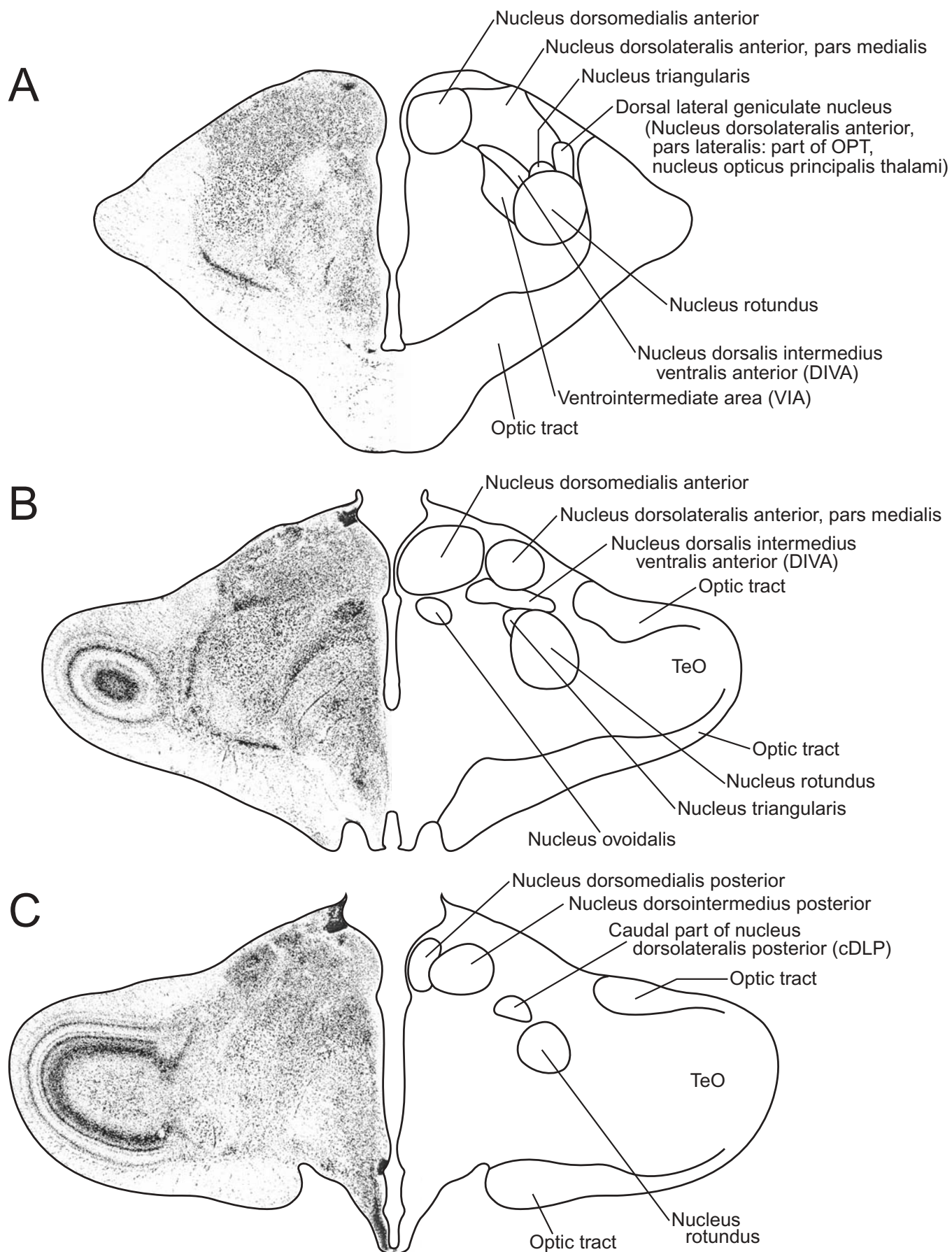


FIGURE 22-11. Transverse hemisections with mirror-image drawings through the diencephalon of a bird (*Columba livia*). The top section (A) is the most rostral. Abbreviation: TeO, optic tectum. Adapted from Karten and Hodos (1967) with additional data from Arends and Zeigler (1991), Wild (1987b), and Medina et al. (1997) and used with permission of The Johns Hopkins University Press.

TABLE 22-1. Dorsal Thalamic Nuclei of Mammals, as Exemplified by Primates (based on Jones, 1985)

Nuclear Group	Name (and Abbreviation) of Nucleus	Main Nonneocortical Afferent Sources	Main Efferent Projections
Geniculate Nuclear Group	Dorsal lateral geniculate nucleus (DLGN or LGN)	Retina	Striate cortex
	Medial geniculate nucleus, pars ventralis (MGNv)	Inferior colliculus	Primary auditory cortex
	Medial geniculate nucleus, pars dorsalis (MGNd)	Inferior colliculus	Association auditory cortices
	Medial geniculate nucleus, pars medialis (MGNm)	Inferior colliculus	Primary and association auditory cortices
Lateral Nuclear Group	Lateral posterior nucleus (LP)	Visual layers of superior colliculus	Extrastriate visual cortices
	Pulvinar, inferior part (PI)	Visual layers of superior colliculus	Extrastriate visual cortices
	Pulvinar, lateral part (PL)	Visual layers of superior colliculus	Extrastriate visual cortices
	Pulvinar, medial part (PM)	Intermediate layers of superior colliculus	Extrastriate visual cortices, frontal eye fields, and higher-order cortices
	Pulvinar, anterior part (PA) [probable equivalent of posterior medial nucleus (POm) of cats and rodents]	Spinothalamic system and possibly dorsal column nuclei	Parietal cortices, possibly including somatosensory regions
Posterior Nuclear Group	Suprageniculate nucleus (SG)	Deeper layers of superior colliculus	Insular cortex
	Limitans nucleus (LI)		
	Posterior nucleus (PO)	Dorsal column nuclei, spinothalamic system, intercollicular region, and inferior colliculus	Retroinsular and postauditory cortices
Ventral Nuclear Group	Nucleus ventralis anterior, pars parvicellularis (VApc)	Globus pallidus, internal segment (see Chapter 24)	Frontal lobe cortices and cingulate motor cortex
	Nucleus ventralis anterior, pars magnocellularis (VAmc)	Substantia nigra pars reticulata	Caudal and medial orbital cortices
	Nucleus ventralis lateralis, pars oralis (VLo)	Globus pallidus, internal segment	Supplementary and premotor cortices and cingulate motor cortex
	Nucleus ventralis lateralis, pars caudalis (VLc)	Cerebellar nuclei	Primary motor cortex
	Nucleus ventralis lateralis, pars medialis (VLm)	Globus pallidus, internal segment	
	Nucleus ventralis posterior, ventral posterolateral part, pars oralis (VPLo)	Cerebellar nuclei	Primary motor cortex
	Nucleus ventralis posterior, ventral posterolateral part, pars caudalis (VPLc)	Dorsal column nuclei and spinothalamic tract	Primary somatosensory cortex
	Nucleus ventralis posterior, ventral posteromedial part, principal part (VPM)	Trigeminal sensory nuclei	Primary somatosensory cortex
	Nucleus ventralis posterior, ventral posteromedial part, pars parvicellularis (VPMpc)	Gustatory nucleus	Primary taste cortex (Brodmann's area 43)
	Nucleus ventralis posterior inferior (VPI)		Secondary somatosensory cortex

TABLE 22-1. (Continued)

Nuclear Group	Name (and Abbreviation) of Nucleus	Main Nonneocortical Afferent Sources	Main Efferent Projections
Midline Nuclear Group	Paratenial nucleus (pt)	Hypothalamus (?)	Amygdaloid nuclear complex and anterior cingulate cortex
	Paraventricular nucleus (pv)		
	Reuniens nucleus (Re)		
	Rhomboidal nucleus (Rh)		
	Median central nucleus (Mc)		
Rostral Intralaminar Nuclear Group	Paracentral nucleus (Pc)	Multiple sources, including the striatopallidal complexes (see Chapter 24), superior colliculus, pedunculopontine tegmental nucleus, cerebellar nuclei, spinal cord, and reticular formation	Topographically to widespread areas of neocortex
	Central lateral nucleus (Cl)		
	Central median nucleus (Cm)		
Caudal Intralaminar Nuclear Group	Centre médian nucleus (CM)		Dorsal striatum and ventral striatum (see Chapter 24) and topographically to widespread areas of neocortex
	Parafascicular nucleus (Pf)		
	Subparafascicular nucleus (sPf)		
Medial Nuclear Group	Dorsomedial nucleus (DM)	Amygdaloid nuclear complex, basal forebrain, olfactory cortex, and olfactory bulb	Prefrontal cortex
Anterior Nuclear Group (Limbic Thalamic Nuclei)	Anteroventral nucleus (AV)	Mammillary nuclei, as well as brainstem structures, including raphe and pedunculopontine tegmental nucleus	Cingulate gyrus and related cortical areas
	Anterodorsal nucleus (AD)		
	Anteromedial nucleus (AM)		
	Lateral dorsal nucleus (LD)		
		Pretectum and lateral hypothalamus	

anterior lateral nucleus or both of these nuclei are homologous to the dorsal posterior nucleus of other Group I anamniotes remains to be resolved.

Somatosensory afferents to the midbrain roof have not been studied in most anamniotes. In frogs, ascending projections from the spinal cord and the region of the obex, where the dorsal column nuclei are located, terminate in the midbrain roof. It has been postulated that somatosensory (and possibly multisensory) projections are present from the midbrain roof to a region within the area of the central and lateral (anterior and posterior) nuclei (Fig. 22-5), but their exact locus of termination is not yet known.

Group IIA

Tectal efferent projections have not yet been studied in hagfishes. In Group II cartilaginous fishes, the optic tectum projects to the **dorsal posterior nucleus**. The dorsal posterior nucleus projects to the dorsal striatum and/or to the pallidum. More studies are needed to clarify the details of this pathway. The dorsal posterior nucleus in teleost fishes (Fig. 22-8) receives tectal projections and projects predominantly to the dorsal striatum (the dorsal nucleus of area ventralis, Vd). In goldfishes but not other teleosts, it also has been found to project to the medial part of the pallidum, Dm.

Group IIB

In placental mammals, the **lateral nuclear group** includes one or more nuclei that receive a major input from the visual layers of the superior colliculus—the **lateral posterior nucleus** (LP) and/or parts of the **pulvinar** [Fig. 22-9(C-F)], depending on the species. The visual tecto-recipient nuclei are often referred to as **LP/pulvinar (LP/pul)** for simplicity. The part of the pulvinar that receives the tectal visual input is the inferior pulvinar; the pulvinar includes additional nuclei that do not receive input from the superior colliculus. The LP/pulvinar complex receives topographic projections from the superior colliculus and projects primarily to extrastriate visual cortical areas in the telencephalon. It also projects to the dorsal striatum (the caudate nucleus-putamen). A homologue of the LP/pulvinar of placental mammals has not yet been identified in monotremes.

In placental mammals, the dorsal thalamus also contains a **posterior nuclear group** [Fig. 22-9(E)]. Among mammals, the posterior nuclear group is best developed in primates. (The medial part of the posterior group, or Pom, receives lemniscal trigeminal input; it therefore appears to belong instead to the ventral nuclear group.) Two components of the posterior nuclear group, the **suprageniculare nucleus** and the **limitans nucleus** (which are sometimes referred to collectively as the limitans/suprageniculare complex), receive substantial

TABLE 22-2. Terminology Used for Dorsal Thalamic Nuclei in Amniotes

	Mammals	Reptiles	Birds
Lemniscal Visual Nuclei	Dorsal lateral geniculate nucleus (DLGN)	Dorsal lateral geniculate nucleus (DLGN)	Dorsal lateral geniculate nucleus (DLGN)—also called nucleus opticus principalis thalami (OPT)
Lemniscal Somatosensory and Related Nuclei	Ventral nuclear group (and medial part of posterior nuclear group: Pom)	Within nucleus dorsolateralis anterior (DLA)	Nucleus dorsalis intermedius ventralis anterior (DIVA) and ventrointermediate area (VIA)
Limbic System Related Nuclei	Anterior nuclear group	Within nuclei dorsolateralis anterior (DLA) and dorsomedialis (DM)	Within nuclei dorsolateralis anterior (DLA) and dorsomedialis (DM)
Rostral Nuclei with Diverse Inputs	Rostral, medial intralaminar nuclei	Within nucleus dorsolateralis anterior (DLA), nucleus dorsomedialis (DM), and perirotundal nuclei	Medial and dorsal parts of nucleus dorsomedialis anterior (DMA), nucleus dorsomedialis posterior (DMP), and subhabenular nucleus
Olfactory Relay Nucleus	Mediodorsal nucleus	Possibly within DM or DLA	Lateral part of DMA and DMP
Caudal, Lateral Nuclei with Diverse Inputs	Caudal, lateral intralaminar nuclei (parafascicular nucleus and the paracentral and central lateral nuclei)	?	Nucleus dorsointermedius posterior thalami (DIP) and the nuclei dorsolateralis anterior thalami, pars medialis (DLM) and dorsolateralis posterior thalami (DLP), respectively
Midbrain Auditory Relay Nuclei	Medial geniculate body	Nucleus medialis (M), also called nucleus reuniens pars compacta (RE)	Nucleus ovoidalis (O)
Midbrain Visual and Somatosensory-Multisensory Relay Nuclei	Lateral posterior-pulvinar complex (LP/pulvinar), limitans/suprageniculate complex, lateral part of posterior nuclear group (Pol), and additional posterior intralaminar nuclei	Nucleus rotundus (R), nucleus medialis posterior (MP) (called the medialis complex in crocodiles and nucleus caudalis in turtles) and nucleus reuniens pars diffusa	Nucleus rotundus (R), caudal part of nucleus dorsolateralis posterior (cDLP), and nucleus semilunaris parovoidalis

tectal input, as does the **lateral part of the posterior nuclear group**, or Pol. This tectal input to the posterior nuclear group arises particularly from the deeper layers of the superior colliculus and thus includes somatosensory projections and multisensory (auditory-somatosensory or auditory-somatosensory-visual) components.

The suprageniculate nucleus and some other neighboring nuclei in this same caudal region of the dorsal thalamus, including the **medial, magnocellular part of the medial geniculate nucleus**, are sometimes referred to as **posterior intralaminar nuclei**. These nuclei share a pattern of tectal afferents combined with widespread projections to neocortex and are thus best viewed as additional components of a posterior/intralaminar system of nuclei. There is also an individual **posterior intralaminar nucleus** in this region, which has a pattern of afferent and efferent connections similar to that of the other posterior group nuclei. It projects, along with the other components of the posterior group, to multimodal, association areas of the neocortex, as well as to the dorsal striatum. Not all of these nuclei (including the posterior intralaminar, subparafascicular, and peripeduncular nuclei) are listed in Table 22-1.

Another telencephalic target of these visual and multimodal collothamic nuclei in mammals also needs to be noted here. In addition to their projections to parts of neocortex and to the dorsal striatum, the medial parts of both the lateral posterior nucleus and the pulvinar, along with the posterior intralaminar nuclei, project to the **lateral nucleus of the amygdala**. This nucleus is a component of the basolateral amygdala and has extensive interconnections with the frontal and temporal association cortices (see Chapters 19 and 25).

In reptiles and birds, the most prominent thalamic nucleus receiving substantial tectal visual projections is called **nucleus rotundus** (Fig. 22-10 and 22-11). It is a large nucleus and has a round shape in all planes of section. Tectal visual projections also terminate in a nucleus, particularly recognized in birds, called **nucleus triangularis**, which medially borders nucleus rotundus. Nucleus rotundus and nucleus triangularis both project to a circumscribed area within the dorsal ventricular ridge (separate from the auditory projection area) and also to the dorsal striatum. In birds, the rotundal-receptive part of the dorsal ventricular ridge is called the entopallium. This collothamic visual pathway is topographically organized in birds but possibly not in reptiles.

The somatosensory-recipient, multisensory part of the midbrain roof in reptiles projects to an area of the dorsal thalamus that lies in the same region as nuclei rotundus, triangularis, and ovoidalis and has been given a variety of names. It is referred to here as **nucleus medialis posterior** (Fig. 22-10), as it has been designated in lizards. This cell group alternatively is called the **medialis complex** in crocodiles or **nucleus caudalis** in turtles (see Table 22-2). Nucleus medialis posterior projects both to the dorsal striatum and to a discrete region within the dorsal ventricular ridge, a region that lies between the visual- and auditory-recipient areas of the ridge. A neighboring nucleus, **nucleus reuniens pars diffusa** (not shown in Fig. 22-10), also receives midbrain roof input and projects to an area of the dorsal ventricular ridge neighboring that of the medialis projection and also interposed between the visual and auditory recipient areas.

In birds, similarly located and connected nuclei are present in the dorsal thalamus. One of these nuclei, the homologue of nucleus medialis posterior, is referred to as the **caudal part of nucleus dorsolateralis posterior**, or **cDLP** (Fig. 22-11). The second nucleus (not shown in Fig. 22-11) borders nucleus ovoidalis. It is the homologue of nucleus reuniens pars diffusa and is called either **nucleus semilunaris parovoidalis** or the **ventromedial part of nucleus ovoidalis**. These nuclei predominantly receive somatosensory and multisensory inputs from the midbrain roof and project to the dorsal ventricular ridge.

In discussing the collothamic visual and multisensory nuclei of mammals above, we noted that these nuclei project to a total of three targets in the telencephalon, one of which is the dorsal striatum within the subpallium and two of which are pallial—parts of neocortex and the lateral nucleus of the amygdala. In contrast, in sauropsids, most studies have noted only two telencephalic targets of the visual/multisensory collothamic nuclei: the dorsal striatum in the subpallium (which is clearly homologous to the dorsal striatum of mammals: see Chapters 19 and 24) and a cell population located within the anterior part of the dorsal ventricular ridge (ADVR). Of continuing debate, therefore, is whether the collothamic-recipient regions within the ADVR of sauropsids are homologous to the collothamic-recipient parts of neocortex, or to the collothamic-recipient lateral amygdalar nucleus, or to both, or to neither.

Identifying homologous relationships between dorsal thalamic nuclei would contribute substantially to resolving this crucial question, but the issue likewise has remained a major point of contention at the thalamic level. Some support the idea that nucleus rotundus is homologous to the LP/pulvinar complex, implying homology of ADVR with components of neocortex. Others support the idea that nucleus rotundus and the other collothamic visual and multisensory nuclei are homologous to the posterior and posterior intralaminar set of nuclei, implying homology of the ADVR to the lateral amygdalar nucleus. Another suggestion has been that the ADVR is unique to sauropsids and cannot be compared with any structure in the mammalian telencephalon. The only remaining logical possibility—that the ADVR corresponds to both the collothamic neocortex and the lateral amygdalar nucleus as a field homology—also has been broached. In this regard, it should be noted that the assignment of LP/pulvinar to the collothalamus has

been questioned. Because the controversy concerns embryological evidence that is not definitive and because its strong tectal afferent input clearly indicates collothamic affinity, it is treated as such here. The evolutionary origin of LP/pulvinar might be a critical key to understanding the relationship of the ADVR in sauropsids to the collothamic neocortex and/or the lateral amygdala of mammals. We will return to this challenging and fascinating conundrum in Chapter 25, where we will consider the evolution of these pallial regions in further detail.

LEMNOTHALAMUS

One nucleus in anamniotes, **nucleus anterior**, and a diverse array of nuclei in amniotes, particularly mammals, receive their predominant input from structures other than the midbrain roof. Multiple inputs have been found for these nuclei, including a prominent retinal projection and lemniscal somatosensory projections. Other inputs include minor ones from the midbrain roof and those related to the hypothalamus and limbic system. Additionally, particularly in amniotes, some lemnothalamic nuclei are involved in motor feedback circuitry linking the striatopallidal complexes and the cerebellum with motor cortices. The lemnothalamic nuclei also appear to have a significant serotonergic input from the raphe as a common characteristic.

Group I

In lampreys, the optic tract lies on the lateral (superficial) edge of the diencephalon and terminates on the dendrites of dorsal thalamic neurons in the rostral diencephalon (Fig. 22-2), but thalamotelencephalic projections remain to be studied. In squalomorph sharks, retinal axons terminate on the dendrites of a nucleus in the rostral part of the dorsal thalamus, nucleus anterior (Fig. 22-3), which also receives a minor tectal projection. As we will discuss below, nucleus anterior projects to the dorsal and/or medial pallium in some Group II sharks and in skates, but it has only a sparse projection to the medial pallium in squalomorph sharks. In nonteleost ray-finned fishes, the retina projects to a dorsal thalamic nucleus, nucleus anterior (Fig. 22-4), which also receives minor tectal projections. At least in reedfishes, nucleus anterior does not appear to project to any part of the pallium, but it may project to the striatal region of the subpallium.

In salamanders and lungfishes, in which almost no migration of neurons occurs, retinal axons terminate on the lateral aspect of the thalamus, but they terminate mostly in ventral thalamic sites rather than extending into dorsal thalamic territory. Also in frogs (see Box 22-1), the retinal axons terminate mostly within the ventral thalamus. In salamanders and lungfishes, the dorsal thalamic cell groups are not separated into discrete groups, but in frogs, several nuclei can be distinguished in Nissl-stained material. The most rostral zone of the dorsal thalamus in frogs (Fig. 22-5) contains nucleus anterior, which receives multiple inputs from a large variety of sources, including direct tectal input, additional tectal input relayed via a nucleus in the posterior thalamus, ascending somatosensory

input from the dorsal column nuclei and the spinothalamic system, ascending auditory input, and projections from the ventral part of the hypothalamus and the medial pallium. The most substantial projection from nucleus anterior is an ipsilateral one to the medial pallium and the medial part of the dorsal pallium. Some of the neurons that contribute to this projection also give off branches that project to the contralateral medial

pallium. Nucleus anterior also projects ipsilaterally to the optic tectum, the posterior dorsal thalamus, the hypothalamus, and to several limbic system-related sites in the more ventral part of the telencephalon, including parts of the amygdala, ventral striatum, and septum. The projection to the septum is to its lateral part and, like the projection to medial pallium, is bilateral.

BOX 22-1. Evolutionary Origin of the Lemnothalamic Visual Pathway: New Perspectives

Gerhard Roth and his co-workers have investigated the anatomy and physiology of the dorsal thalamus in a salamander, *Plethodon jordani*, and a frog, *Bombina orientalis*, and found that a lemnothalamic visual pathway may not be present in amphibians. Contrary to previous views that nucleus anterior receives direct retinal input and relays it to the pallium, they found that nucleus anterior cells receive scant if any direct retinal input. In electrophysiological studies, they showed that the neurons within

nucleus anterior do not receive monosynaptic or disynaptic input from the retina; instead, they receive mostly inhibitory inputs, most likely from neurons within the ventral thalamus. The main efferent projection from nucleus anterior is to the medial pallium bilaterally, with some projections to the ipsilateral dorsal pallium as well. One of the neurons that projects to the medial and dorsal pallia is shown in Figure 1. As is the case in this instance, some of these cells have a few dendritic processes that extend into ventral

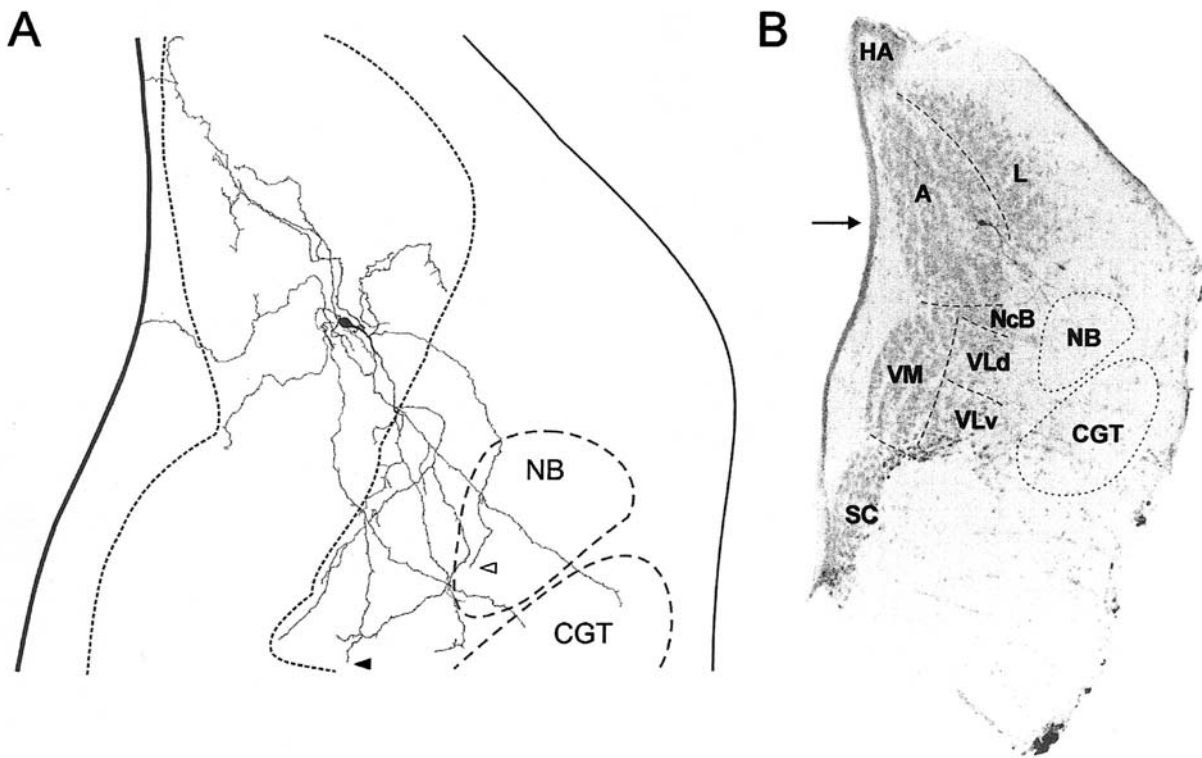


FIGURE 1. Drawing (A) of a neuron within nucleus anterior of the fire-bellied toad, *Bombina orientalis*, that projects to the medial and dorsal pallia. The neuron was visualized after intracellular injection of biocytin. The actual section is shown in B, with the location of the filled neuron indicated by the arrow. For both A and B, the midline is toward the left and dorsal is toward the top. Abbreviations: A, nucleus anterior; CGT, corpus geniculatum thalamicum; HA, habenula; L, lateral dorsal nucleus; NB, neuropil of Bellonci; NcB, nucleus of Bellonci; VLd, dorsal portion of ventrolateral nucleus; VLv, ventral portion of ventrolateral nucleus; VM, ventromedial nucleus; SC, suprachiasmatic nucleus. The latter is part of the hypothalamus; excepting it, A and L, and the habenula, all other nuclei listed here are components of the ventral thalamus. From Roth et al. (2003) and used with permission of John Wiley & Sons.

BOX 22-1. Evolutionary Origin of the Lemnothalamic Visual Pathway: New Perspectives—cont'd

thalamic areas where retinal axons terminate (labeled NB for neuropil of Bellonci and CGT for corpus geniculatum thalamicum), but the nucleus anterior neurons are not significantly influenced by any possible minor retinal input that may occur thereby.

Based on only sparse tectal afferentation, efferent connections to medial pallium, and topographic position, the nucleus anterior in amphibians is clearly lemnothalamic; however, as Roth and his co-workers discuss, it more closely resembles the mammalian anterior, dorsomedial, and anterior midline nuclei, as well as the more rostral intralaminar nuclei, rather than the dorsal lateral geniculate nucleus. As we will discuss below, these nongeniculate nuclei are all limbic or limbic-related lemnothalamic components. Two possible evolutionary scenarios could account for the lack of a lemnothalamic visual pathway in amphibians: either such a pathway was absent in the ancestral tetrapods and evolved in amniotes, or such a pathway was present ancestrally and has been lost in amphibians. The absence of a pallial projection from nucleus anterior in reedfishes, which are cladistian ray-finned fishes, might be taken to indicate that a lemnothalamic visual pathway was indeed absent ancestrally. However, the pallium of reedfishes is one of the best examples of a Type I brain that exists, with extreme lack of migration of neuronal cell bodies away from the juxtaventricular layer. If this pathway could be lost in amphibians, it also could have been lost in cladistians. Studies are needed in both Type II ray-finned fishes and cartilaginous

fishes in order to reexamine whether their retinorecipient rostral dorsal thalamus, i.e., nucleus anterior, consistently gives rise to pallial projections.

As discussed further below, in the lizard *Podarcis hispanica*, Natalia Kenigfest and her colleagues reexamined the retinorecipient thalamus and precisely identified the set of neurons that receive direct retinal input and project to the visual lemnothalamus, both in this lizard and in other reptiles based on a review of the literature. Thus, in at least some reptiles, the visual lemnothalamic pathway is present, as it also is in birds and in mammals.

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Group IIA

In hagfishes (Fig. 22-6), one of the dorsal thalamic nuclei, nucleus anterior, may be homologous to the same-named nucleus in other anamniotes; it receives retinal projections. In Group II cartilaginous fishes—galeomorph sharks, skates, and rays—some migration of neurons also occurs in the dorsal thalamus. A nucleus anterior has been identified in some species and lies within the area labeled dorsal thalamus in Figure 22-7. This nucleus receives direct retinal projections. Likewise in most teleosts (Fig. 22-8), nucleus anterior receives a major projection directly from the retina. Minor tectal projections have also been found to the nucleus anterior in sharks and teleosts. Nucleus anterior is known to project to the central nucleus of the dorsal pallium in sharks (primarily contralaterally) and bilaterally to the medial pallium in skates, although its total pattern of projections has yet to be studied in any cartilaginous fish. In teleosts, nucleus anterior lies most rostrally, and it receives predominantly retinal input. Only in goldfishes, it has been found to project bilaterally to the dorsolateral (distal) part of the pallium.

Group IIB

Mammals. In placental (eutherian) mammals, not only multiple nuclei but multiple groups of nuclei characterize the

dorsal thalamus. Although marsupial mammals have many of the same nuclei as placental mammals, we will focus on the dorsal thalamus of placental mammals in this section for the sake of simplicity, with some comments on the dorsal thalamus of monotremes for contrast.

In placental mammals (Fig. 22-9), the lemnothalamus comprises four major groups of nuclei that lie in the rostral dorsal part of the thalamus and the dorsal lateral geniculate nucleus, which is categorized separately. Three of the lemnothalamic nuclear groups are the anterior, medial, and ventral nuclear groups. The fourth group consists of part of the intralaminar nuclear group and associated midline nuclei. All of the main intralaminar nuclei (as defined by Edward Jones in his 1985 book on the dorsal thalamus) were initially identified as components of the lemnothalamus, but recent findings of substantial tectal projections to some of them indicate a revision of that position, as discussed below. We will first consider the dorsal lateral geniculate nucleus and the anterior and ventral nuclear groups, as they are the most straightforward of the lemnothalamic components. We will then consider the medial and the lemnothalamic intralaminar and midline nuclei, as they share certain features and seem to form a natural grouping.

In monotremes and placental mammals (as well as in marsupials), a substantial retinal projection terminates in the **dorsal lateral geniculate nucleus**. The term geniculate

means knee-like, and in most primates, the layers of this nucleus bend to form a U-shape. This nucleus also receives a minor input from the superior colliculus (optic tectum). The dorsal lateral geniculate nucleus projects topographically to the ipsilateral striate (visual) cortex. It also receives a reciprocal projection from striate cortex that far exceeds the retinal input in synaptic density. Within the dorsal thalamus, the dorsal lateral geniculate nucleus lies in a more caudal position in the dorsal thalamus of placental mammals than it does in monotremes or than does the homologous dorsal lateral geniculate nucleus in sauropsids, due in large part to the more extensive development of the other parts of the lemnothalamus, particularly the anterior nuclear group, in placental mammals and the consequent caudal displacement of the dorsal lateral geniculate nucleus.

The most rostrally located group of nuclei in the dorsal thalamus of placental mammals, the **anterior nuclear group**, comprises several nuclei—**anteroventral**, **anterodorsal**, and **anteromedial**. These nuclei are part of limbic system circuitry, linking the hypothalamus and other structures with limbic-related regions of neocortex as well as directly with the hippocampus. One of the traditionally named components of the lateral nuclear group, the **lateral dorsal nucleus**, is now also included in the anterior group, due to its juxtaposed position and its obvious kinship in terms of limbic system connections. It projects heavily and topographically to parts of the ipsilateral medial (limbic) cortex, particularly the cingulate cortex. In at least some mammals and in accord with the tendency of lemnothalamic telencephalic projections to be bilateral, the anteromedial nucleus additionally projects to the contralateral cortex. Afferent input to the anterior nuclear group arises primarily in the medial pallium and in a part of the ventral hypothalamus called the mammillary bodies. This anterior nuclear group has also been found to receive a sparse input from the retina in a variety of species. In monotremes, only a single **anterior nucleus** is present, and its connections are unknown.

The **ventral nuclear group** consists of two major components. One component comprises two main nuclei, the **ventral posterolateral (VPL)** and **ventral posteromedial (VPM) nuclei**, which receive lemniscal somatosensory inputs. VPL receives ascending somatosensory inputs from the dorsal column nuclei (fine touch and proprioception) and the spinothalamic system (pain and temperature), while VPM receives similar inputs from the trigeminal system that originate in the principal sensory nucleus and the descending, or spinal, nucleus of the trigeminal, respectively. An ascending gustatory projection also terminates in part of the ventral posterior nuclear group. The somatosensory portion of the ventral nuclear group projects topographically to the ipsilateral somatosensory cortex.

The second component of the ventral nuclear group comprises the **ventral anterior** and **ventral lateral nuclei**, which each have subdivisions (see Table 22-1) and are sometimes collectively referred to as the **motor thalamus**. The ventral anterior nucleus receives input from the internal segment of the globus pallidus and the substantia nigra pars reticulata (see Chapters 17 and 24), while the ventral lateral nucleus receives inputs from the internal segment of the globus pallidus and the deep cerebellar nuclei. The ventral anterior and ventral lateral

nuclei project to motor-related areas of the neocortex. Part of the nuclear area that receives input from the pallidum, substantia nigra, and gustatory system projects bilaterally to frontal and medial cortices. The ventral lateral nucleus, which receives cerebellar and pallidal inputs, projects to ipsilateral motor cortex. A large area of the dorsolateral thalamus has been identified as the somatosensory relay area in monotremes.

The **medial nuclear group** has several components in placental mammals. Its most prominent nucleus is the **mediodorsal**, or **dorsomedial, nucleus** [Fig. 22-9(C and D)]. This nucleus is distinguished by its receipt of a substantial afferent input from the olfactory cortex. It also receives projections from the mesencephalic reticular formation and the amygdala. The mediodorsal nucleus projects to the ipsilateral prefrontal and prelimbic cortices. Recently, it also has been found to project to transitional orbital and medial cortices in the contralateral telencephalon. Thus, the mediodorsal nucleus provides a bilateral relay of olfactory information to nonolfactory areas of the dorsal pallium. In monotremes, a mediodorsal nucleus that projects to the prefrontal cortex is also present.

The **midline nuclear group** in placental mammals has been less extensively studied than most other dorsal thalamic nuclear groups, due in part to its position and the small size of some of its component nuclei. It includes the **medioventral nucleus** [Fig. 22-9(A)], which is sometimes called the **reuniens nucleus**, since it is continuous across the midline. This nucleus, which is listed in Table 22-1 by the latter name, has reciprocal connections with the medial pallium in addition to an input from the lateral pallium (olfactory cortex). It can be regarded as related more to the anterior group than to the medial group because of the similarity of its connections with the medial pallium. Some of the other midline nuclei, such as the **parataenial nucleus**, share a pattern of diverse inputs and widespread cortical projections with the intralaminar nuclei. Among the midline nuclei in monotremes, a medioventral (reuniens) nucleus has been identified.

The **intralaminar nuclear group** comprises multiple nuclei. These nuclei receive inputs from diverse sources, including a number of hindbrain and midbrain cell groups, and they give rise to widespread projections to neocortex. For placental mammals, Table 22-1 lists the main set of six intralaminar nuclei, divided into rostral and caudal groups. Not included in this grouping are the so-called posterior intralaminar nuclei, which were considered above in conjunction with the posterior nuclear group.

In placental mammals, the main set of intralaminar nuclei all receive input from diverse sources, including the cortex, striatopallidum, superior colliculus (optic tectum), pretectum, spinal cord, and a number of sites in the brainstem. The latter are primarily related to the motor system and include nucleus cuneiformis, the reticular formation, and the substantia nigra. The intralaminar nuclei give rise to projections that terminate in widespread areas of the telencephalon, including bilateral projections to transitional cortices. The intralaminar nuclei also project to the dorsal striatum and are thus involved in striatopallido-thalamostriatal circuitry (see Chapter 24). Monotremes apparently lack a parataenial nucleus and most or all intralaminar nuclei, however; no nucleus has been found that gives rise to widespread telencephalic projections.

It should be noted that, although the intralaminar projection to cortex is widespread, it is not diffuse in the sense of individual neurons giving rise to single axons that branch and terminate across widespread cortical regions. Rather, the intralaminar nuclei comprise a set of discretely projecting cell populations that in totality blanket the cortex. Low-frequency stimulation of the intralaminar nuclei produces a set of repetitive, negative electrical waves in the cortex, as monitored by electroencephalographic (EEG) recordings, called the **cortical recruiting response**. Spontaneous cortical rhythms are suppressed during the response, and the EEG is like that taken during sleep. Conversely, higher frequency stimulation of the intralaminar nuclei produces an EEG pattern similar to a state of wakefulness. Thus, the intralaminar nuclei modulate and regulate the state of arousal. In placental mammals, the integrity of the intralaminar system is required for the maintenance of the conscious state. Interestingly, since monotremes apparently lack this system, they may have alternate pathways that subserve the same function (and see Chapter 13).

While three of the intralaminar nuclei—the central medial, rhomboid, and centre médian—are clearly lemnothalamic, the rest may be collothalamic. On the basis of recent findings of input to these nuclei from the superior colliculus, it has been suggested that three of the main set of intralaminar nuclei—the parafascicular, paracentral, and central lateral nuclei—are collothalamic rather than lemnothalamic. As in the case of the dorsal lateral geniculate nucleus, light collicular input is not diagnostic for collothalamic assignment, but while the collicular input to the paracentral nucleus is rather light, as is the case for most other intralaminar nuclei, the collicular input to the parafascicular and central lateral nucleus is substantial. This distinction is noted here as the basis for comparisons discussed below with various nuclei in the sauropsid dorsal thalamus.

Nonmammalian Amniotes. In the more rostral part of the thalamus in sauropsids, a nucleus that predominantly receives retinal projections and projects to the telencephalic pallium is present. This nucleus has been variably named in the literature or in some papers not identified at all, but it is now clear that it comprises the homologue of the mammalian **dorsal lateral geniculate nucleus**, or **DLGN**, and we thus will refer to it by that name in reptiles (Fig. 22-10). In birds, it often has been referred to as **OPT**, the **nucleus opticus principalis thalami**, and it comprises several separately named cell groups. We will refer to it here in birds (Fig. 22-11), as well as in reptiles, as the dorsal lateral geniculate nucleus.

Several ventral thalamic nuclei that are constituents of the ventral lateral geniculate nuclear complex (see Chapter 19) lie immediately ventral to the dorsal lateral geniculate nucleus, and the dorsal-most of these has been identified previously as a homologue of the DLGN, due in part to the close proximity of these cell groups and their shared feature of a substantial afferent retinal projection. The term nucleus intercalatus and the term dorsal lateral optic nucleus¹ both refer to this dorsal-most component of the VLGN.

¹In Figure 22-9 of the first edition of this textbook, the area indicated as the dorsal lateral optic nucleus was incorrectly thought to be part of the dorsal thalamus, but more recent findings indicate that it is actually part of the ventral thalamus. The dorsal lateral geniculate nucleus lies dorsomedial to this position, as shown in this edition (Fig. 22-10).

The dorsal lateral geniculate nucleus receives a substantial retinal input and other lesser inputs, including a minor input from the optic tectum. In reptiles, this nucleus projects ipsilaterally to an area in the dorsolateral part of the pallium called the pallial thickening (in lizards, snakes, and crocodiles) or to the lateral part of the dorsal cortex (in turtles). In birds, the dorsal lateral geniculate nucleus projects bilaterally to the visual Wulst (visual hyperpallium). In birds, this thalamotelencephalic pathway is known to be topographically organized. Reciprocal pallial projections to the DLGN also have been found in turtles and birds.

Two other nuclei are present in the rostral and dorsal part of the dorsal thalamus in reptiles (Fig. 22-10)—**nucleus dorsolateralis anterior** (DLA) and **nucleus dorsomedialis** (DM). These nuclei receive a more diverse set of connections than the DLGN. In lizards, DLA receives somatosensory inputs from both the dorsal column and the trigeminal systems in addition to a variety of other sensory system inputs, including the spinal cord, torus semicircularis, hypothalamus, other thalamic nuclei, and the septum. It also receives a serotonergic input from the raphe and a sparse retinal projection. Widespread areas of the telencephalon receive projections from DLA, including the medial cortices, the dorsal cortex including its lateral part, the pallium thickening, the lateral cortex, and, in turtles, the striatum. The projection of DLA to the pallial cortices is bilateral.

DM also receives a diverse array of inputs in lizards, including afferents from the spinal cord and the raphe, but with more of an emphasis on visceral sensory, hypothalamic, and limbic cell groups rather than the more somatically-related DLA. Like DLA, DM has widespread telencephalic projections to cortical areas, the dorsal ventricular ridge, and the striatum.

In birds (Fig. 22-11), more than two nuclei have been identified in the region occupied by DM and DLA in reptiles. Two of these nuclei, **nucleus dorsomedialis anterior thalami** (DMA) and **nucleus dorsolateralis anterior thalami pars medialis** (DLM) lie dorsal to nucleus rotundus and thus form part of a “shell” region around it. Other nuclei complete the shell around the more ventral aspects of nucleus rotundus, and this set of nuclei is referred to collectively as the **perirotundal nuclei**. A direct projection to DM from the olfactory cortex recently has been found in birds.

Two additional, separately named nuclei of this same region are recognized in birds—the **nucleus dorsalis intermedialis ventralis anterior** (DIVA) and a more ventrally situated nucleus, the **ventrointermediate area** (VIA) (Fig. 22-11). DIVA is the thalamic relay for the somatosensory system. It receives input from the dorsal column nuclei, and it projects bilaterally to a somatosensory portion of the Wulst within the telencephalic pallium. This pathway is the same as the dorsal column-nucleus ventral posterolateral-somatosensory cortex pathway in mammals. A separate nucleus with similar connections has not yet been found in reptiles, although a ventromedial part of the perirotundal nuclei (DLA/DM) may be homologous to DIVA as part of a field, since ascending somatosensory projections have been found to this area. VIA receives inputs from motor-related structures, including the globus pallidus, cerebellar nuclei, and the substantia nigra. It thus resembles the ventral lateral nucleus of mammals and its position in the basal ganglia-cerebellar feedback path-

ways through the thalamus to motor-related regions of the cortex and the ventral anterior nucleus in its combination of pallidal and substantia nigra afferentation (see Chapter 24). Other nuclei are also present in the region of the thalamus in birds. As discussed further below, a **dorsal thalamic zone**, or **DTZ**, has been recognized that includes DMA and DLM along with a number of other nuclei, including nuclei dorsomedialis posterior thalami (DMP), dorsointermedius posterior thalami (DIP), dorsolateralis posterior thalami (DLP), and subhabenularis lateralis (SHL). This set of nuclei correspond in position, connections, histochemistry, and other traits to the mammalian intralaminar, midline, and mediodorsal nuclei. As noted below, both lemnothalamic and collothalamic elements are present within this grouping.

EVOLUTIONARY PERSPECTIVE

Collothalamus

A sensory relay nucleus of the dorsal thalamus that receives input from the torus semicircularis (inferior colliculus) and projects to the telencephalon is present in all vertebrates studied. Depending on the taxon, this nucleus is variously called the central posterior nucleus, nucleus medialis, nucleus reuniens pars compacta, nucleus ovoidalis, or the medial geniculate body. Like the optic tectal relay nucleus, this nucleus projects predominantly to the ipsilateral striatum and modestly to the pallium in amphibians. Additionally, it projects robustly to the pallium in amniotes. The presence of this nucleus and its projection to the ipsilateral striatum is thus plesiomorphic for at least jawed vertebrates, and its substantial projection to the pallium in amniotes is apomorphic.

A sensory relay nucleus of the dorsal thalamus that receives input from the optic tectum (superior colliculus) and projects to the telencephalon has been found in all vertebrates studied except monotremes. Various called the dorsal posterior nucleus, the anterior lateral nucleus, or nucleus rotundus in nonmammalian vertebrates, this nucleus projects ipsilaterally to the striatum in all taxa studied. In some cartilaginous fishes and in sauropsids, this nucleus also projects robustly to the pallium. A dorsal thalamic nucleus receiving tectal projections and projecting to the ipsilateral striatum is thus plesiomorphic for at least jawed vertebrates. The addition of substantial projections of the nucleus to the pallium has occurred twice independently, in sharks and in amniotes.

Relay nuclei of the dorsal thalamus that receive somatosensory and multisensory input from the optic tectum and project to the telencephalon have been found in all sauropsids. An area of the dorsal thalamus with similar connections is postulated to be present in frogs. Among sauropsids, these nuclei are called nucleus medialis posterior and the pars diffusa of nucleus reuniens and nucleus dorsolateralis posterior and nucleus semilunaris parovoidalis or the ventromedial part of nucleus ovoidalis. Such nuclei appear to be plesiomorphic for at least amniotes and also appear to be homologous, at least as a field, to a part of the dorsal thalamus of amphibians in the region of the central and lateral nuclei.

In mammals, controversy exists as to the homologue of the visual tecto-recipient, pallial projecting nucleus—i.e., the

nucleus rotundus of sauropsids. LP/pulvinar has long been regarded as its homologue, but some argue that nucleus rotundus, along with nucleus medialis posterior and the other tecto-recipient nuclei noted above, are all homologous to parts or all of the posterior nuclear group/posterior intralaminar nuclei of mammals. As further information is gained on the embryological development and genetic markers of LP/pulvinar and the constituents of the posterior nuclear group and neighboring nuclei, it is hoped that this issue can be resolved.

Lemnothalamus

A single nucleus in the rostral thalamus, nucleus anterior, is present in anamniote vertebrates. This nucleus has been found to receive a substantial retinal input and a lesser tectal input in fishes. In amphibians, it receives multiple inputs, including projections from the tectum directly and the posterior thalamus relaying tectal input, the ventral hypothalamus, the medial pallium, and somatosensory and auditory structures, and it projects bilaterally to the medial and dorsal pallia. It does not receive a retinal input, however. Nucleus anterior is plesiomorphic for at least jawed vertebrates and probably all vertebrates. The bilateral projections of the nucleus to the medial pallium may also be plesiomorphic for vertebrates or they may have evolved independently in cartilaginous fishes and tetrapods. The presence of multiple inputs from diverse, non-visual sources, including a somatosensory input, to nucleus anterior is apomorphic for tetrapods. Its lemnothalamic relay of retinal inputs to the pallium may occur only in amniotes or have been lost ancestrally in amphibians.

The nucleus dorsolateralis anterior of reptiles projects bilaterally to the medial pallium and to other cortical areas as well. It receives input from diverse sources, including a sparse retinal input and somatosensory inputs from the dorsal column and trigeminal systems. Its bilateral projection to the medial pallium and its diverse inputs are similar to the connections of the nucleus anterior of some anamniotes. Nucleus dorsomedialis projects diffusely to the ipsilateral pallium and striatum, and it receives a spinal input. The spinal input to nucleus dorsomedialis is similar to that of nucleus anterior of anamniotes, and its diffuse projections include the medial pallium to which nucleus anterior likewise projects in amphibians and some cartilaginous fishes. Both nucleus dorsolateralis anterior and nucleus dorsomedialis lie in the rostral thalamus. These two nuclei may therefore be homologous as part of a field to the nucleus anterior of anamniotes.

Anton Reiner and his colleagues Loreta Medina and Leo Veenman recently identified what they term the **dorsal thalamic zone**, or **DTZ**, in birds, which comprises several nuclei that are homologous as a set to parts of the dorsolateral and dorsomedial nuclei of reptiles: nuclei dorsomedialis anterior thalami (DMA), dorsomedialis posterior thalami (DMP), dorsolateralis anterior thalami pars medialis (DLM), dorsointermedius posterior thalami (DIP), dorsolateralis posterior thalami (DLP), and subhabenularis lateralis (SHL). They compared the avian DTZ to the intralaminar, midline, and mediodorsal complex of nuclei, or **IMMC**, in mammals. They proposed that SHL and the medial and dorsal parts of the avian DMA and DMP can be compared to the midline and medially lying intralaminar nuclei of mammals and that the lateral parts of DMA and

DMP can be compared to the mediodorsal nucleus. These nuclei are thus clearly lemnothalamic and in all likelihood homologous to the anterior nucleus of anamniotes. In contrast, they compared the avian DIP to the parafascicular nucleus of mammals and the avian DLM and DLP to the laterally lying paracentral and central lateral nuclei of mammals, all of which are now regarded as collothamic nuclei. The major distinction here involves where to draw the boundary line between lemnothalamic and collothamic territory. As noted above and based on recent findings of a substantial tectal input, the more lateral parts of the intralaminar nuclei of mammals may be collothamic (as are clearly the posterior intralaminar nuclei related to the posterior nuclear group), and the same designation appears to apply to the comparable regions of the thalamus in sauropsids as well. Other recent studies in both birds and reptiles support the basic comparison of most of DM and DLA in sauropsids to many of the lemnothalamic nuclei of mammals.

Also included in this general group of lemnothalamic nuclei is the nucleus dorsalis intermedius ventralis anterior (DIVA) of birds, which receives ascending, lemniscal somatosensory input from the dorsal column nuclei. As in the case of nucleus dorsomedialis, this input is similar to that of the nucleus anterior of amphibians. The projections of DIVA to the dorsal pallium are bilateral in birds, similar to the bilaterality of the projections of the nucleus anterior of some anamniotes. Afferent somatosensory projections that originate in both the trigeminal and dorsal column nuclei have likewise been found to the dorsolateral anterior nucleus in lizards. Another nucleus in birds that lies immediately ventral to DIVA, the ventrointermediate area (VIA), has related connections that are motor feedback in nature. It receives major inputs from the cerebellar nuclei, the substantia nigra, and the basal ganglia (see Chapter 24) and is thus comparable to the ventral anterior and ventral lateral nuclei of mammals, which have similar connections. Thus, both the avian DIVA and VIA appear to be homologous to part of the dorsolateral anterior nuclear region of reptiles and thus also homologous to the ventral nuclear group of mammals—the ventral posterior, ventral anterior, and ventral lateral nuclei.

Likewise, the dorsal lateral geniculate nucleus of reptiles and birds receives a substantial lemniscal retinal input, as does the nucleus anterior of fishes. Among sauropsids, its projections to the pallium are bilateral in birds but only ipsilateral in reptiles.

From these data, it would appear that the dorsal lateral geniculate nucleus is also homologous as part of a field to the nucleus anterior of anamniotes. Since a lemniscal somatosensory cell group has been found within the dorsolateral-dorsomedial nuclei in reptiles in a comparable location to the same nucleus in birds, this nucleus likewise appears to be part of the field that is homologous to the nucleus anterior of anamniotes. In other words, the same embryonic anlage that gives rise to nucleus anterior in anamniotes gives rise to the major portions of nucleus dorsolateralis anterior and nucleus dorsomedialis region of reptiles, which includes the lemniscal somatosensory nucleus and, at least in birds, the motor-feedback relay nucleus, as well as to the dorsal lateral geniculate nucleus. The lateral migration of neurons during the development of the dorsal thalamus and the presence of multiple

nuclei as opposed to a single nucleus anterior are apomorphic for amniotes.

The anterior nuclear group of placental mammals [and the anterior and medioventral (reuniens) nucleus of monotremes] receives inputs from the medial cortex and the hypothalamus, as well as a sparse retinal input. This group projects to the ipsilateral medial cortex, and part of it additionally projects bilaterally to the cortex. The medially and rostrally lying set of intralaminar nuclei has diverse inputs and projects diffusely to the pallium and striatum; this diffuse projection is predominantly ipsilateral, but some projections to the contralateral telencephalic cortex are present as well.

Connections similar to the olfactory afferent connections of the mammalian mediodorsal nucleus, which projects to prefrontal neocortex, resemble the projection to nucleus dorso-medialis from olfactory cortex in birds. The target of the mediodorsal nucleus in mammalian prefrontal cortex is hallmarked by a very dense innervation of ascending dopaminergic fibers, and regions that are similarly densely innervated by dopaminergic fibers have been identified in the dorsal pallium of both lizards and birds. Thus, an olfacto-thalamo-dorsal pallial pathway may be present in most or all amniotes. Taken as a whole, the connections of the anterior, medial, and the mediorostral intralaminar nuclei of mammals resemble those of the dorsolateral and dorsomedial nuclei of sauropsids and those of nucleus anterior in amphibians.

These various lemnothalamic nuclei in mammals and in sauropsids, generally located in the rostral part of the dorsal thalamus, thus can be hypothesized to be homologous, as the products of a homologous developmental field, to the nucleus anterior of anamniotes. Projections to the telencephalon from these nuclei that are only ipsilateral, instead of bilateral, are apomorphic where present, although the possibility exists that some of the bilateral projections present in amniotes may have been first lost and then reevolved. Projections from these nuclei to the striatum are apomorphic for amniotes.

The ventral nuclear group and the dorsal lateral geniculate nucleus lie in the caudal part of the dorsal thalamus in placental mammals. This caudal position may be secondarily due to the relative expansion of the anterior, medial, and intralaminar nuclear groups. The connections of a large part of the mammalian ventral nuclear group and the dorsal lateral geniculate nucleus are similar to those of the somatosensory relay nuclei (where present) and the dorsal lateral geniculate nucleus of sauropsids, respectively. The afferent connections of these nuclei are also similar to some of the afferent connections of the nucleus anterior of anamniotes. These data suggest that the dorsal lateral geniculate nucleus of mammals is homologous as a discrete nucleus to the dorsal lateral geniculate nucleus of sauropsids. The mammalian ventral nuclear group and the dorsal lateral geniculate nucleus are also homologous as a field, along with the anterior, medial, and mediorostral intralaminar nuclei, to the nucleus anterior of anamniotes.

In the captorhinomorph amniotes (Fig. 22-1), which gave rise to all extant amniote vertebrates, increased cell proliferation during development resulted in an abundance of migrated nuclei in the dorsal thalamus. In the ancestral line of the placental mammals, continued expansion of the lemnothalamus occurred, and a number of nuclear groups, rather than single nuclei, were formed. The relative expansion of the anterior,

medial, and intralaminar groups of nuclei resulted in a relative, caudal displacement of the ventral nuclear group and the dorsal lateral geniculate nucleus within the dorsal thalamus.

A NEW DEFINITION OF THE DORSAL THALAMUS IN VERTEBRATES

Some previous definitions of the dorsal thalamus of vertebrates have been based primarily on features of the mammalian dorsal thalamus. One of the frequently used criteria for a dorsal thalamic nucleus has been that it must project to a specified cytoarchitectonic area within the neocortex or limbic cortex or to their homologues. As we discussed above, collothamic nuclei project predominantly to the striatum in anamniotes. The projections of lemnothalamic nuclei to the pallium are frequently bilateral, rather than just ipsilateral, in anamniotes and amniotes alike, although to a lesser degree in mammals. Substantial projections to the pallium, in addition to projections to the striatum, are an apomorphy of collothamic nuclei in amniotes, as are projections to the striatum from some of the lemnothalamic nuclei, i.e., the lemnothalamic intralaminar nuclei, in amniotes. The distributions of topographic organization of various pathways through the dorsal thalamus and of reciprocal connections from the pallium to the dorsal thalamus need further investigation in a variety of species, but neither is a defining feature of a dorsal thalamic nucleus.

Difficulties in recognizing the cytoarchitectonic areas of the dorsal thalamus must also be considered. The neurons of nuclei derived from one embryonic anlage may migrate or be displaced to a different region within the adult brain. For example, the pregglomerular nuclear complex lies near the area of the dorsal thalamus in fishes, as discussed in Chapter 20. Thus, to distinguish nuclei in the region of the dorsal thalamus from other diencephalic nuclei, such as ventral thalamic, pretectal, or pregglomerular nuclei, on the basis of the presence or absence of a projection to the telencephalon is hazardous at best. Nuclei derived from other sources, such as the hypothalamus in some fishes, also serve as relay nuclei to the telencephalon (as will be discussed in Chapter 23). The pulvinar in humans, but not in other primates or any other vertebrate, contains a population of neurons that have migrated from the telencephalon.

The definition of the dorsal thalamus that is proposed here is as follows: *the dorsal thalamus of jawed vertebrates comprises those nuclei that are derived from the embryonic dorsal thalamic anlage, belong to one of two fundamental divisions that are based on the source of the predominant afferent input, receive input predominantly from the contralateral sensory world, and project to the striatum or to the pallium or to both.* Dorsal thalamic nuclei may have either specifically or nonspecifically (widespread) organized projections, may or may not have projections that are topographically organized, may or may not receive reciprocal projections from the telencephalon, and may project to the telencephalon bilaterally or only ipsilaterally. Diencephalic nuclei other than those of the dorsal thalamus may also project to the telencephalon.

The key event that is hypothesized to have occurred in the development of the dorsal thalamus in the ancestral stock of extant amniote vertebrates, that is, in the captorhinomorphs

(Fig. 22-1), was an increase in the number of neurons produced by the dorsal thalamic germinal matrix in conjunction with migration of the earlier-produced neurons away from the area of the matrix. This developmental change occurred for both the lemnothalamic and collothamic divisions, resulting in the formation of multiple, discrete, migrated nuclei within both divisions: a dual elaboration of the dorsal thalamus.

With the more lateral position of a number of nuclei in captorhinomorphs, additional changes occurred as well. The collothamic nuclei increased their projections to the pallium from minor to substantial ones, in addition to retaining their projections to the striatum. Some of the lemnothalamic projections to the contralateral pallium were lost. Projections to widespread areas of both the pallium and striatum from some lemnothalamic and some collothamic nuclei were gained. More changes then occurred within the separate radiations of mammals (synapsids) and of the sauropsids (reptiles and birds), including a shift to a relatively caudal position of the visual and somatosensory lemnothalamic nuclei in mammals due to extensive secondary expansion of the rest of the lemnothalamus.

A number of apomorphic features of dorsal thalamic nuclei were acquired in ancestral amniotes, as were additional ones in marsupial and placental mammals. The selective pressures encountered in a terrestrial habitat, as opposed to an aquatic one, favored the establishment of these features. Lateral migration of the neurons of the sensory relay nuclei is correlated with a marked increase in the number of subdivisions of these nuclei and the importance of visual, auditory, and somatosensory cues in the terrestrial world.

The elaboration of the anterior nuclear group of mammals into multiple nuclei and the shift of this system from a multisensory relay to, in effect, a cortical-thalamo-cortical circuit (with the additional relay through the mammillary bodies) may have been correlated with the increased use of the medial (limbic) cortex in learning and memory. All vertebrates have ascending sensory system relays, but in mammals in particular and to some extent in birds, the analysis and use of this sensory information by the limbic system appear to have vastly increased. The expansion and elaboration of medially lying nuclei in amniotes, such as the medial nuclear group and the intralaminar nuclei, is correlated with adaptation to the terrestrial environment.

As is the case in many regions of the brain (such as the pretectum, the posterior tuberculum, the hypothalamus, and various parts of the telencephalon), the dorsal thalamus has evolved differently in different radiations of vertebrates. Within the diencephalon of nontetrapods, the pretectum and posterior tuberculum are among those regions that are most elaborated and expanded. In contrast, the dorsal thalamus is most elaborated and expanded in amniotes and, within amniotes, in placental mammals. The differential elaboration of different parts of the central nervous system reflects the variety of adaptations in the various radiations of vertebrates that have evolved in response to the demands of new and changing habitats.

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23

The Visceral Brain: The Hypothalamus and the Autonomic Nervous System

INTRODUCTION

The viscera are the contents of the four main body cavities: the cranium, the thorax, the abdomen, and the pelvis. Used in a strict sense, the term “visceral” thus refers to the internal body organs. Indeed, elsewhere in this book, we have used the term visceral in its strict sense and will do so again later in this chapter when we discuss the autonomic nervous system. We now, however, must introduce the use of “visceral” in a more general sense; that is, referring to a wide variety of biological processes that psychologists would classify as “emotion” and “motivation” and that zoologists would classify as survival behavior for the individual and the species. Individual survival behaviors include finding and obtaining the basic necessities of life: food, water, maintenance of body temperature, and shelter from unfavorable environmental situations. Species-survival behaviors include courtship, defense of territory, mate selection, and parental care of the young. The visceral brain, both in the narrow sense and in the wider sense of the term, includes the **hypothalamus**. In addition to interacting with the autonomic nervous system, the hypothalamus has important connections with sensory systems such as the olfactory system and the visual system. In addition to the hypothalamus and the autonomic nervous system, we will also discuss the **area preoptica** (sometimes spelled **praeoptica**) or **preoptic area**, which is a transitional area between the diencephalon and the telencephalon.

In this chapter, we will first discuss the hypothalamus in anamniotes. We have not divided anamniotes into Group I and Group IIA for two reasons. First, the cytoarchitecture of the hypothalamus does not vary between these groups as much as

do a number of other parts of the central nervous system. Second, less information about the connections and functions of the hypothalamus is available than is the case for many other brain regions in anamniotes. We then will discuss the hypothalamus of amniotes and will end with a description of the autonomic nervous system.

The Hypothalamus

In the majority of the brain regions we have encountered thus far, we have found nuclear groups that have more or less discrete boundaries. Some of these boundaries are formed by a sheath of myelinated or sometimes unmyelinated axons that sharply delimits a neuronal population from the surrounding tissue. In other cases, the neurons' sizes, shapes, or other characteristics distinguish a cell population from its neighbors. In the hypothalamus, however, some of the neuronal populations do not have a discrete appearance and therefore merge with or overlap their neighboring neuronal groups; hence, they are known as “areas” rather than “nuclei.” Two such examples are the *lateral hypothalamic area* and the *preoptic area*. In addition, like the thalamus, the hypothalamus consists of a large number of nuclei with similar sounding names. Some are variations on the directional terms “medial,” “lateral,” “dorsal,” and “ventral.” Other names are descriptive of location or appearance, such as “supraoptic” (meaning “above the optic tract”) or “arcuate” (meaning “having an arc-like shape”). A further complication, as in the thalamus and elsewhere in the central nervous system, is that various scientists have tended to use somewhat different nomenclature to identify these cell groups. Where differing nomenclatures have been used, we have tried

to use the most common name and to mention alternative names that refer to the same group of neurons.

We also note the presence of a unique feature of the diencephalons of sharks, teleosts, and other fishes: the **saccus vasculosus**, which is an outpouching of the **hypothalamic ventricle**, which is itself an extension of the third ventricle. Several functions for this structure have been suggested, including a pressure-detection organ, a chemosensory organ, an osmoregulatory organ, and an ionic transport mechanism. The presence of parathyroid hormone-related protein (PTHrP) in this structure suggests a role in skeletal growth, tooth regeneration, calcium transport, kidney function, insulin expression, or any of the other biological functions association with this protein. Any or all of these may be correct. Clearly, more needs to be learned about this important hypothalamic organ. The saccus vasculosus is connected to the **nucleus sacci vasculosi** in the posterior tuberculum by the **tractus sacci vasculosi**.

The Hypothalamus and the Endocrine System

The hypothalamus is closely associated with the **endocrine system** because of its intimate relationship with the **pituitary** or **hypophysis** (Greek for an undergrowth), which is located just below the floor of the hypothalamus. An area known as the **eminentia medialis** or **median eminence** is located at the zone of attachment between the hypothalamic floor and the hypophysis. The hypophysis itself is divisible into two main regions: the more posterior, which is called the **neurohypophysis** or **pars nervosa**, and the more anterior, which is called the **adenohypophysis**, from the Greek word, *aden*, meaning a gland. A third division, the **pars intermedia**,

is actually a component of the adenohypophysis. The neurohypophysis is in continuity with the hypothalamus proper, and, as its name implies, it consists of neural tissue. The neurohypophysis receives the terminals of peptide-secreting neurosecretory cells that have their somata in the hypothalamus. The secretions of these neurosecretory cells enter the circulatory system and are transported to target organs such as the kidney and the reproductive system.

The adenohypophysis is composed of three subdivisions: the most posterior region called the **pars intermedia** or intermediate part; a middle region called the **pars tuberalis** or **tuberal region**; and the most anterior division, the **pars distalis** or **anterior lobe**. The pars tuberalis is sometimes known as the **pars infundibularis** because of its association with the **infundibulum**, which is Latin for “little funnel” and is the stalk by which the pituitary is attached to the hypothalamus. The adenohypophysis, unlike the neurohypophysis, is a complex endocrine gland. The adenohypophyseal or anterior pituitary hormones travel through the general circulation to specific target organs, some of which are endocrine glands, such as the thyroid or the gonads, others of which are nonendocrine glands, such as the mammary glands of mammals, and still others that are general organ systems, such as the skeleton or the pigment cells of the skin.

As shown in Figure 23-1, the morphology of the hypophysis varies considerably across vertebrate classes. Several features not found in tetrapods characterize the hypophysis of sharks and teleost fishes. One feature is the presence of finger-like projections of the neurohypophysis into the adenohypophysis. Neurons of the hypothalamus enter the adenohypophysis via these projections. Finally, teleosts and lampreys lack an eminentia medialis, although hormones can

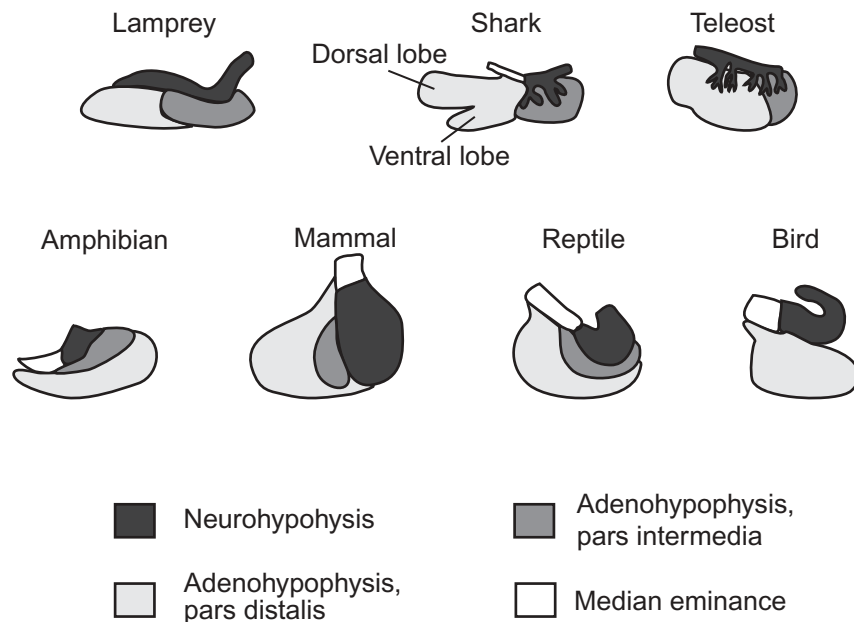


FIGURE 23-1. Various forms of the hypophysis among vertebrate classes. Note the absence of a median eminence in lampreys and teleosts and the absence of a pars intermedia of the adenohypophysis in birds. In sharks and teleosts, the neurohypophysis sends finger-like protrusions into the adenohypophysis. Adapted from Leim et al. (2001) and used with permission of Thomson Learning Global Rights Group.

migrate by diffusion directly from the hypothalamus in these animals. The eminentia medialis is present in sharks and chondrosteian fishes. A unique feature of the hypophysis of elasmobranchs is the division of the pars distalis into a **dorsal lobe** and a **ventral lobe**.

Among the features that characterize the hypophysis of tetrapods is the loss of the finger-like projections of the neurohypophysis into the adenohypophysis. Two curious features exhibited by the hypophysis across vertebrates are the absence of a pars intermedia in birds and the absence of a median eminence in teleost fishes.

The pituitary serves as the link between the hypothalamus and the general circulatory system that allows neuropeptides and monoamines produced in the hypothalamus and median eminence to affect the various target tissues. Two mechanisms of linkage exist: a direct linkage and an indirect linkage. As shown in Figure 23-2, the linkage to the neurohypophysis or posterior pituitary is direct; neurosecretory neurons in the hypothalamus send their axons through the median eminence and infundibulum to terminate in the neurohypophysis where their secretions of **oxytocin** and **vasopressin** are introduced into the general circulation via a network of capillaries. Both oxytocin and vasopressin (the latter also known as antidiuretic hormone) belong to superfamilies of related hormones that have similar effects in different groups of vertebrates. Thus, oxytocin belongs to the superfamily that includes **isotocin** in fishes and **mesotocin**, which is found in amphibians, reptiles, and birds. Vasopressin similarly belongs to the superfamily that includes **vasotocin**, which is its homologue in nonmammals. These hormones have effects on the kidney in all vertebrates, and they also are important in certain aspects of social behavior in mammals and other vertebrate classes as well. Additionally, oxytocin affects the transport of ova and reproductive behavior in amniotes in general and causes contractions of the uterus and the flow of milk in mammals. As is the case for many other hormones, these families of hormones have multiple effects, which are too numerous and too variable across classes to enumerate in greater detail here.

Also shown in Figure 23-2 is the indirect linkage in which the neurosecretory neurons terminate in the median eminence. The secretions of these neurons are known as **releasing hormones** and **inhibiting hormones**. These substances are picked up by capillaries and transported via an intrinsic hypophyseal circulatory network known as the **hypophyseal portal system**, which is present in all vertebrates except lampreys and teleost fishes. In these animals, the hypothalamic hormones enter the adenohypophysis by diffusion.

Some of these hypothalamic hormones stimulate the release of anterior pituitary hormones, and others inhibit their release. The hormones of the anterior pituitary, their releasing

and inhibiting hormones, and their target tissues are listed in Tables 23-1 and 23-2. The pituitary hormones, in addition to their well-known effects on peripheral organs of the body, are also neuroactive substances at a number of locations in the brain. The reader might find a comparison of Tables 23-1 and 23-2 with Table 2-1, which lists some of the many neuroactive substances, to be useful at this point. In addition to serving as neuroactive substances in the brain, many of these hypothalamic and pituitary hormones serve more than one function. For example, **prolactin** is involved in electrolyte balance in ray-finned fishes, metamorphosis in amphibians, and milk production in mammals, and it also plays a role in parental care in many vertebrates.

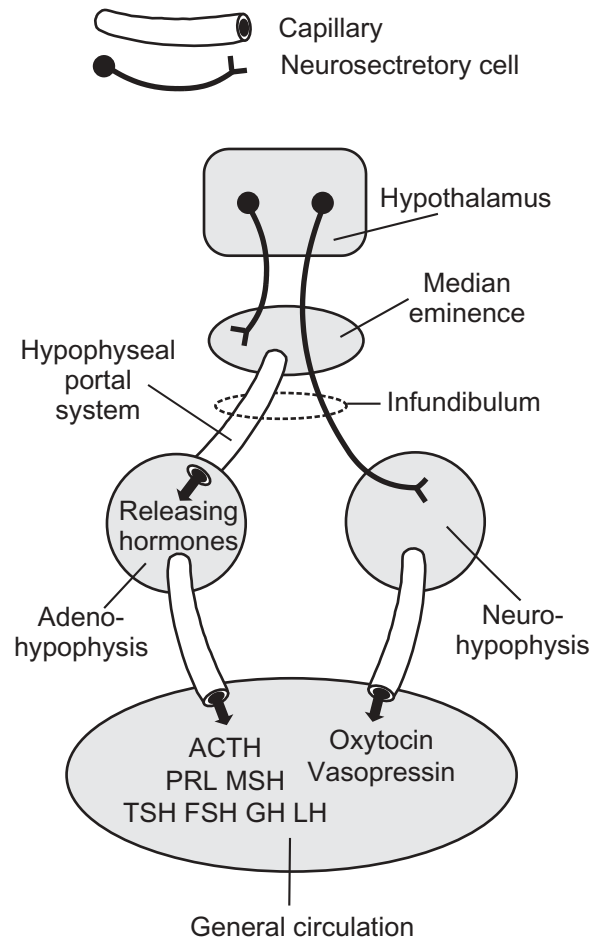


FIGURE 23-2. A schematic diagram of the hypothalamic hypophyseal portal system.

TABLE 23-1. Some of the Major Hypothalamic and Anterior Pituitary Hormones That Regulate Endocrine Glands

Hypothalamic Releasing Hormone	Pituitary Hormone	Target Endocrine Gland
Gonadotropic releasing hormone (GnRH)	Follicle stimulating hormone (FSH), luteinizing hormone (LH)	Testis, ovary
Corticotropin releasing hormone (CRH)	Adrenocorticotrophic hormone (ACTH)	Adrenal cortex
Thyrotropin releasing hormone (TRH)	Thyroid stimulating hormone (TSH)	Thyroid, oviduct (reptiles, birds)

BOX 23-I. Hypothalamic Peptides and Proteins

In addition to the releasing hormones and trophic hormones described above, other hormones have recently become the objects of much scientific interest because of the newly emerging evidence of their roles in the regulation of food intake, reproduction, sleep, and other hypothalamic functions. Some of these compounds are produced in the hypothalamus, some in the pituitary, and some in the gut or in fat cells. Several of these substances affect levels of neuropeptide Y, which is a powerful activator of feeding behavior. The following is a sample of some of these substances and their actions.

The **orexins** (orexin-A and orexin-B), sometimes known as **hypocretins**, comprise a family of hypothalamic neuropeptides that have been implicated in a variety of functions typically associated with the hypothalamus. They have been reported to affect feeding behavior in fishes and to coexist with prolactin in the pituitary of frogs. In birds, they are present in the lateral hypothalamic area (an area related to feeding) during fasting, although they do not stimulate food intake, and they are differentially present in the gonads of males and females. In mammals, orexins result in increased food intake, affect reproduction, alter energy balance, and affect wakefulness and vigilance. We are only just beginning to understand the role of these important peptides in hypothalamic functioning.

Ghrelin, which is produced in the gut, is transported to the hypothalamus by the circulatory system where it regulates growth hormone production in the adenohypophysis. Ghrelin secretion is increased during fasting and it appears to play a role in fat utilization, food intake, and growth. Ghrelin has been reported in teleost fishes, frogs, mammals, turtles, and chickens.

Leptin is a hormone that is produced in fat cells. It is a product of the *ob* gene, which is related to obesity. Leptin is also secreted by the epithelial lining of the gut and the placenta. Like ghrelin, it is transported to the hypothalamus by the circulatory system. Leptin has been found in the medial basal hypothalamus, the preoptic area, the infundibulum and median eminence, as well as in both the adenohypophysis and neurohypophysis.

Melanocortins are another family of peptides that have been reported to have an influence on hypothalamic areas involved in food intake, energy metabolism, and autonomic function. This family includes **adrenocorticotrophic hormone** (ACTH), as well as the **melanocyte stimulating hormones**; all of these are hormones of the adenohypophysis. **Melanocortin-4** receptors play a critical role in obesity and insulin regulation. In goldfishes, the melanocortin system has been associated with the inferior lobe, specifically with the mediobasal hypothalamus, the lateral tuberal nucleus, and the nucleus of the lateral recess.

In rats, melanocortin-4 receptors have been localized in a variety of hypothalamic nuclei including the periventricular, preoptic, paraventricular, posterior, arcuate, and perifornical nuclei, as well as the subfornical organ, which is one of the circumventricular organs to be described in this chapter. A neuropeptide that is related in function to the melanocortins is **urocortin**, which is a corticotrophin releasing factor-like neuropeptide. It decreases food intake in fasting rats possibly by interacting with orexin A. It may also be involved in responses to stress. Corticotrophin releasing factors are reported to affect the paraventricular nucleus of the hypothalamus.

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TABLE 23-2. Some of the Major Hypothalamic and Pituitary Hormones That Regulate Nonendocrine Glands and Organs

Hypothalamic Releasing Hormone	Pituitary Hormone	Some Examples of Target Glands or Organs
Prolactin releasing factor (PRF—also known as vasoactive intestinal polypeptide or VIP), prolactin release-inhibiting hormone (PIH)	Prolactin (PRL)	Ovary (mammals)
		Mammary gland (mammals)
		Skin (reptiles)
		Crop (pigeons and doves)
		Kidney (ray-finned fishes)
Melanocyte stimulating hormone releasing factor (MRF), melanocyte stimulating hormone release-inhibiting factor (MIF)	Melanocyte stimulating hormone (MSH)	Pigment cells
Growth hormone releasing hormone (GHRH), somatostatin (SOM)	Growth hormone (GH)	Skeleton
These hormones are produced in the hypothalamus and are transported to the posterior pituitary where they are secreted. No hypothalamic releasing hormones are involved.	Arginine vasotocin	Kidney and aorta (ray-finned fishes, reptiles, and birds)
		Social behavior (fishes)
		Oviduct (ray-finned fishes, reptiles, birds)
	Isotocin (similar to mesotocin in reptiles and birds and oxytocin in mammals)	Blood vessels and oviduct (ray-finned fishes)
		Social behavior (fishes)
	Oxytocin	Uterus (mammals)
		Mammary gland (mammals), oviduct (reptiles, birds)
		Kidney (ray-finned fishes)
		Social behavior (mammals)
	Vasopressin (antidiuretic hormone)	Kidney, blood pressure
		Social behavior (mammals)

Circumventricular Organs

The third ventricle, like the ventricular system in general, is lined with a thin layer of ependymal cells. In certain regions, however, this layer is thicker and forms specialized organs. These organs, called **circumventricular organs**, contact the cerebrospinal fluid that fills the ventricle and are also innervated by axons, often from hypothalamic and limbic structures. These organs secrete substances into the cerebrospinal fluid, and they can also detect the presence of substances in this fluid. In addition to the circumventricular organs, specialized ependymal cells, known as **tanycytes**, are located in the third ventricle. These cells extend their processes into the substance of the hypothalamus, where they contact blood vessels and neurons. Evidence suggests that tanycytes transport hormones and other substances from the cerebrospinal fluid to the median eminence and possibly other hypothalamic nuclei involved in the production of hypothalamic hormones. Thus, the cerebrospinal fluid circulation may serve as a chemical communication pathway, along with the cardiovascular circulation, in feedback loops that regulate the levels of hypothalamic hormones. Tanycytes also occur elsewhere in the brain

across vertebrates, as noted in the optic tectum of teleost fishes in Chapter 18.

Circumventricular organs are present in all vertebrates, although their number can vary considerably. Anamniotes have four or five; reptiles and mammals typically have six; birds have nine.

The functions of these organs are not well understood. They do, however, seem to play a role in a variety of activities of the visceral brain, such as the regulation of water balance and blood pressure, the monitoring of levels of various trophic hormones and their hypothalamic releasing factors in the cerebrospinal fluid, ingestive behavior, nausea and vomiting, and biological rhythms. Table 23-3 lists the most frequently described organs and gives some indication of their functions as they are presently understood.

Biological Rhythms, the Epiphysis, and the Hypothalamus

Many of the functions of the hypothalamus depend on the daily cycle of light that begins at dawn and ends at dusk. Others

TABLE 23-3. The Major Circumventricular Organs

Organ	Function	Reported in
Vascular organ of the lamina terminalis	Water balance	Birds and mammals
	Blood pressure	
	Reproduction	
Lateral septal organ	Secretes vasoactive intestinal polypeptide (VIP)	Birds
Subfornical organ (called the subseptal organ in nonmammals)	Water balance	Birds, turtles, and mammals
	Blood pressure	
Paraventricular organ	Secretes tropic hormones	Ray-finned fishes, reptiles, and birds
	Water balance	
	Blood pressure	
Median eminence and neurohypophysis	See Tables 23-1 and 23-2	Amphibians, mammals, reptiles, and birds
Pineal	Secretes serotonin and melatonin	All vertebrates
	Biological rhythms	
Subcommissural organ	Secretes glycoproteins	All vertebrates
	Biological rhythms	
Subtrochlear organ	?	Birds
Area postrema	Food aversions	Ray-finned fishes, mammals, reptiles, and birds
	Nausea and vomiting	
	Blood pressure	

depend on the seasonal increases (winter and spring) and decreases (summer and autumn) in the length of the day. The dawn-dusk light cycles are important for some types of **circadian biological rhythms**, which are daily rhythms with a duration of 24 ± 3 h. The longer cycles are important for seasonal rhythms, such as the annual onset of the mating season or annual migrations. Two groups of photoreceptors that have direct connections with the hypothalamus are the retina and the epiphysis or pineal (see Chapters 2 and 21). The axons of the retinal photoreceptors leave the optic tract (see Chapter 26) and enter the hypothalamus where they terminate in the nucleus suprachiasmaticus in the anterior hypothalamus. Electrophysiological and other studies of the suprachiasmatic nucleus suggest that it may serve as the pacemaker for circadian rhythms in conjunction with the pineal.

In some reptiles (as in anamniotes), the pineal functions as a light gathering organ. Its photoreceptors have axons that terminate in the pretectum and tegmentum of the midbrain. In mammals and birds, the pineal's influence on biological rhythms is via the hormone **melatonin**, which is produced in the pineal during the dark phase of the daily light cycle. Concentrations of melatonin also have been reported in the suprachiasmatic nucleus. No evidence of pineal photoreceptors has yet been found in birds or mammals.

The Hypothalamus and the Limbic System

The hypothalamus functions in close association with the limbic system, which will be discussed in detail in Chapter 30.

In brief, the limbic system is involved in emotional and motivational behavior, as well as certain aspects of memory. It is mainly a telencephalic system but has strong connections with the thalamus, hypothalamus, and midbrain tegmentum. The main telencephalic limbic structures that have major connections with the hypothalamus are the **septum**, the **hippocampal formation**, and the **amygdala**. Many structures in the limbic system have receptors for gonadal hormones and are involved in social behaviors that depend on such hormone levels for their timing and expression, such as courtship, territorial defense, aggression, and parental behavior. The limbic system also affects the endocrine system by means of its connections with the hypothalamus.

The Preoptic Area

The preoptic area is a region at the junction of the telencephalon and diencephalon. In keeping with its transition-zone location between two major brain subdivisions, this area plays an important role in the activities of both subdivisions. It is closely related to both the hypothalamus and the limbic system. In particular, the preoptic area is associated with reproductive behavior. It contains many receptor sites for the estrogenic and androgenic sex hormones produced by the testes and ovaries. The preoptic area is one of the regions of the brain that shows **sexual dimorphism**, which means a structural difference between males and females. Other brain areas that also have receptor sites for androgens and estrogens are the hypothalamus and the amygdala.

Maintenance of body temperature within a specific range is important for vertebrates because too low a temperature may slow down the rate at which vital biochemical reactions occur and too warm a temperature can make these reactions occur at too high a rate so that the body's reserves of nutrients and energy are too quickly depleted. Further extremes of heat or cold can result in death. Endothermic animals (mammals and birds) can generate heat internally and regulate temperature by panting, by adjusting the amount of insulating air trapped under feathers or hair, sweating, and other physiological mechanisms. Ectothermic animals, on the other hand, have few or no physiological mechanisms for regulation of temperature, and therefore they regulate their temperature behaviorally by changing their location when the ambient temperature becomes unsatisfactory for their needs. Reptiles possess some physiological mechanisms, such as panting and modification of blood flow at the skin but still must supplement these with behavioral methods to maintain their body temperatures in the optimal range. Whether the thermoregulation is physiological or behavioral, the preoptic area, in conjunction with the posterior hypothalamus, is concerned with regulation of body temperature in amniotes and ray-finned fishes. Insufficient data exist to know whether this area plays an important role in this vital function in amphibians.

THE HYPOTHALAMUS IN ANAMNIOTES

Two major parts of the hypothalamic region are present in all vertebrates: a preoptic area and the hypothalamus proper. The preoptic area is the rostral-most part of the hypothalamic region and is so named because it lies rostral to, or in front of, the optic chiasm. It receives a modest input from the retina in most vertebrates. In anamniotes, the hypothalamus proper can usually be divided into dorsal and ventral parts and may also have several other distinct nuclei.

As discussed in Chapter 21, projections to the preoptic area and the hypothalamus from the epiphysis have been identified in lampreys, ray-finned fishes, and amphibians. These projections along with those from the retina are involved in the control of biological rhythms. Interconnections of the hypothalamus and preoptic area with the habenula are probably also present in anamniotes, although these pathways have been studied in detail only in amniotes.

Jawless Fishes

In lampreys, the hypothalamus constitutes the largest part of the diencephalon. Within it, a **preoptic area** and **dorsal and ventral divisions of the hypothalamus** have been recognized. Although there is a considerable body of data on the neuroendocrinology of the lamprey hypothalamus, relatively few modern reports are available on its cytoarchitecture or connections. It forms a thin shell around the third ventricle. According to available data, the hypothalamus receives afferent axons from all parts of the telencephalon, including the olfactory bulb, from both the tectum and tegmentum of the midbrain, and from the dorsal thalamus. Efferents from the lamprey

hypothalamus are mainly to the tegmentum of the midbrain and the hindbrain, as well as to the dorsal thalamus, ventral thalamus, and the olfactory bulb.

In hagfishes (Fig. 23-3), the preoptic area contains four nuclei: the **periventricular**, **dorsal**, **external**, and **intermediate preoptic nuclei**. The hypothalamus is poorly differentiated, consisting of densely packed cells medially and a more diffuse field of cells caudally that is called the **infundibular nucleus**.

Cartilaginous Fishes

In cartilaginous fishes (Fig. 23-4), a preoptic area is present, and the hypothalamus has a **medial part** surrounding the third ventricle and **inferior lobes**. Telencephalic projections to the preoptic area and the inferior lobes are present. The retina is known to project to the preoptic area in both hagfishes and cartilaginous fishes, as it probably also does in lampreys.

The ventral diencephalon of cartilaginous fishes consists of a large protuberance surrounding the third ventricle, known as the inferior lobe, which is a major component of the hypothalamus. Attached to this lobe, on its ventral surface, is the hypophysis. The hypothalamus is well developed into distinct nuclei that have been recognized in a few species, such as the Type I spiny dogfish shark *Squalus acanthias*. A preoptic nucleus, which projects to the inferior lobe, is present as are a number of other nuclei. Among these is the **suprachiasmatic nucleus**, which receives axons from the optic tract. In many vertebrates, this nucleus is involved in biological rhythms that depend upon the light cycle. The **nucleus medius** caudally replaces the suprachiasmatic nucleus and sends its efferents to the optic tectum, but its afferents are unknown at present. It is relatively larger in Type II cartilaginous fishes, such as the skate *Raja*. In the region of the infundibulum is the **periventricular nucleus**, which projects to the spinal cord, and the **nucleus lateralis tuberis**, which appears to be associated with the hypophysis.

At the lateral expansion of the hypothalamic ventricle within the inferior lobe is the **nucleus lobi lateralis**. This nucleus is connected to the pallial regions of the telencephalon via the **tractus pallii** and to subpallial structures by way of the **basal forebrain bundle**. Other major pathways of the hypothalamus are the **tractus lobobulbaris**, which interconnects the inferior lobe with the hindbrain, especially the reticular formation, and the **tractus lobocerebellaris**, which, as the name indicates, connects the inferior lobe with the cerebellum. Other inputs to the inferior lobe are from the midbrain tegmentum.

Actinopterygians

In ray-finned fishes, the cytoarchitecture, connections, and functions of the preoptic area and hypothalamus have been studied in better detail than in other aquatic anamniotes. Both of these regions contain a number of distinct nuclei. The preoptic region contains an anterior nucleus, the **nucleus preopticus parvocellularis anterioris**, formed by small cells and, as are other nuclei in this region, named for their position and cell size. As shown in Figure 23-5, three nuclei lie caudal to the latter nucleus. **Nucleus preopticus magnocellularis**,

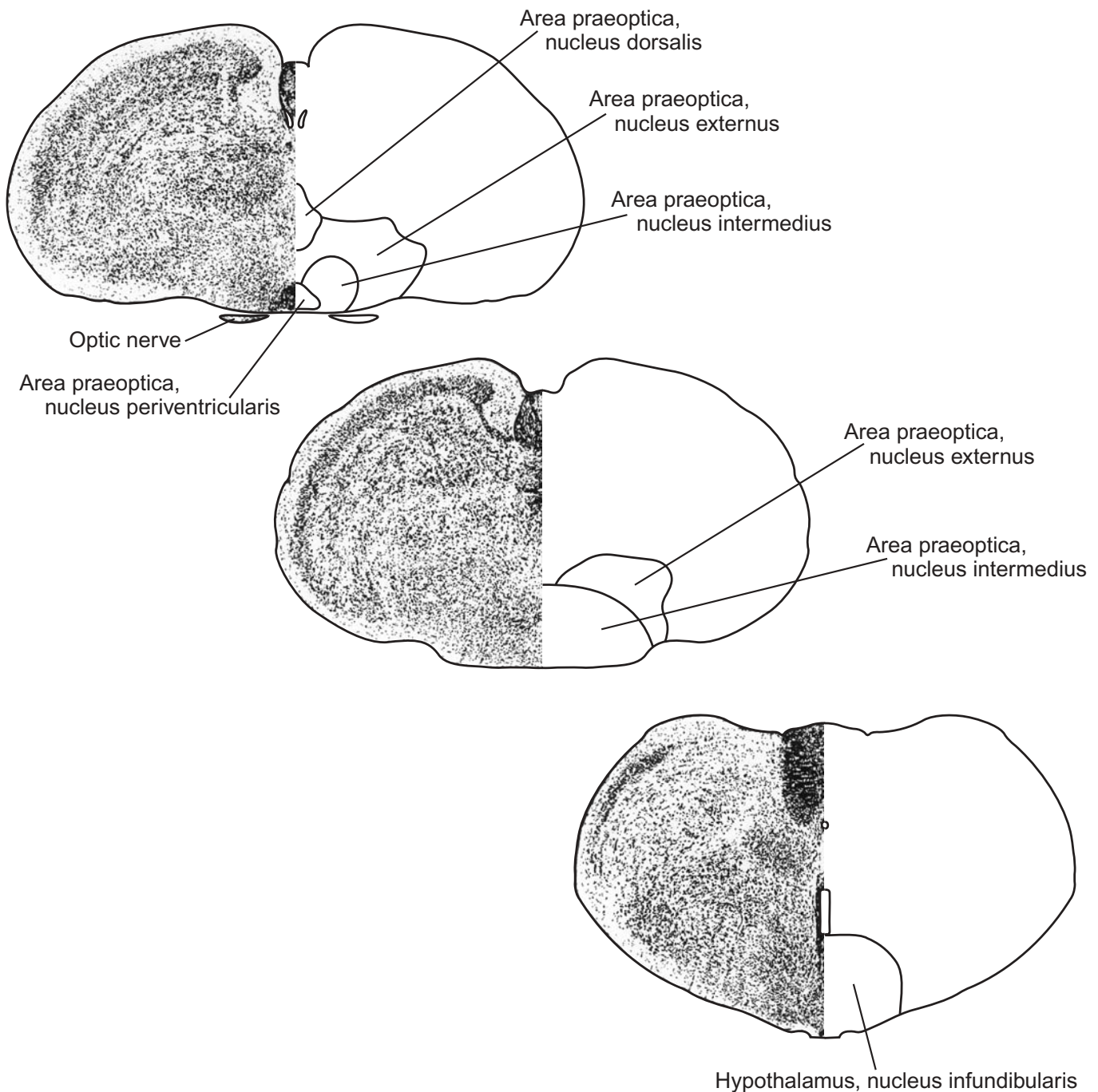


FIGURE 23-3. Transverse hemisections with mirror-image drawings through the diencephalon of a hagfish (*Eptatretus stouti*). The upper hemisection is the most rostral. Adapted from Wicht and Northcutt (1992) and used with permission of S Karger AG, Basel.

named for its large cells, actually contains both large and small celled areas, which are referred to, respectively, as the **pars magnocellularis** and **pars parvocellularis**. A **suprachiasmatic nucleus** is present in the preoptic region and is named for its position dorsal to the optic chiasm. A **nucleus preopticus parvocellularis posterioris** lies ventral to the thalamus caudally.

The part of the hypothalamus that borders the third ventricle is generally divided into dorsal and ventral parts, which are referred to as the **dorsal hypothalamus** and the **ventral hypothalamus**. The hypothalamus also contains other nuclei, some of which are laterally migrated. Three nuclei—the **nuclei ventralis tuberis**, **lateralis tuberis**, and **anterior tuberis**—consist of small aggregations of very

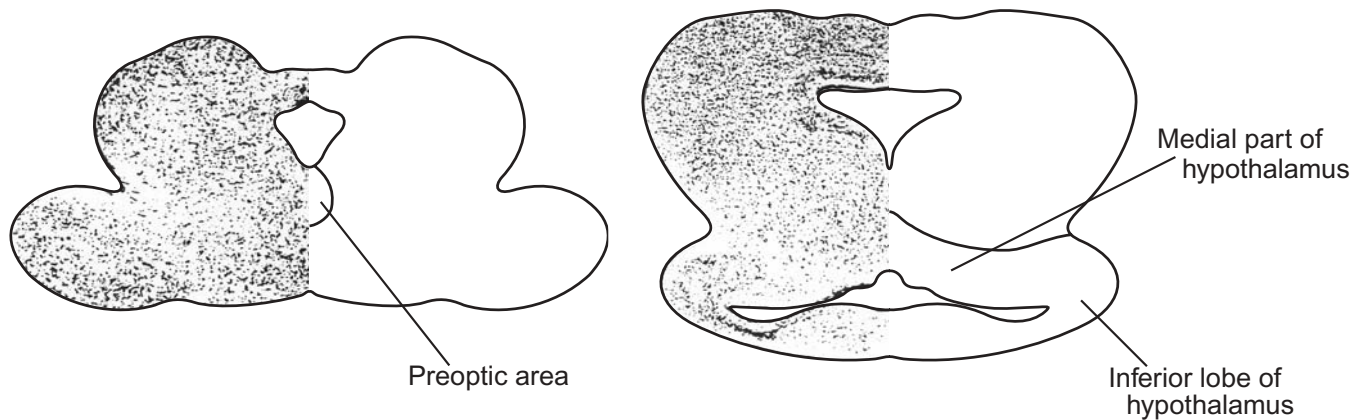


FIGURE 23-4. Transverse hemisections with mirror-image drawings through the diencephalon of a skate (*Raja eglanteria*) and a guitarfish (*Platyrrhinoidis triseriata*). Adapted from Northcutt (1978).

large neurons. In most groups of ray-finned fishes, the inferior lobe is present, into which the hypothalamic ventricle extends. This lobe contains neurons diffusely scattered through it, called **nucleus diffusus of the inferior lobe**, and a smaller, more compact nucleus called **nucleus centralis of the inferior lobe** (Fig. 23-6).

Endocrine Functions. A number of the endocrine functions of the preoptic area and hypothalamus have been studied in ray-finned fishes. Neurosecretory neurons in the preoptic area project to the posterior part of the pituitary gland, the pars nervosa. The pars nervosa interdigitates with a part of the adenohypophysis called the pars intermedia, which releases **melanocyte stimulating hormone**, a hormone that causes dispersion of melanin in melanocytes and consequent darkening of the skin. Neurons in both the preoptic area and hypothalamus are believed to regulate the release of melanocyte stimulating hormone within the pars intermedia. Other preoptic axons that terminate in the pars nervosa release **arginine vasotocin**, a diuretic hormone that increases glomerular filtration in the kidneys and increases blood pressure by causing vasoconstriction in the ventral aorta, or **isotocin**, which acts with arginine vasotocin to increase blood pressure and also causes contraction of the smooth-muscle fibers in the ovary and oviduct during parturition or oviposition.

In teleosts, the part of the adenohypophysis that is known as the pars distalis is directly innervated by axons from the hypothalamus. This situation is different from that in other vertebrates in which a vascular portal system transports hormones from the hypothalamus to the pars distalis. The teleostean pars distalis can be divided into a **rostral zone** that has **prolactin** and **corticotropin**-containing terminals and a more **proximal zone** with **gonadotropin**- and **growth hormone**-containing terminals. **Thyrotropin**-containing terminals occur throughout the pars distalis. Prolactin is important for survival of teleosts in fresh water because it enhances ion concentration and maintains plasma sodium levels. Corticotropin controls blood corticosteroid levels in their normal daily fluctuations and acutely in response to stress. Gonadotropin controls ovulation and ovarian recrudescence, which is a regrowth of the

ovaries that occurs following the release of all mature oocytes (eggs) during spawning, and it also influences sperm production in males. Growth hormone functions as its name implies, and thyrotropin regulates the function of the thyroid gland in controlling metabolic rate.

The release of thyrotropin is regulated by a release-inhibitory hormone secreted by neurons in the anteromedial part of the ventral hypothalamus, while the release of the other hormones of the pars distalis is regulated primarily by the tuberal nuclei. Neurons in the nucleus lateralis tuberis secrete hormones that regulate the release of gonadotropin, prolactin, and corticotropin, the latter also being affected by neurons in the preoptic area. Neurons in the nucleus anterior tuberis may secrete a hormone that affects the release of growth hormone.

Connections of the Preoptic Area and Hypothalamus. In addition to playing a significant role in the regulation of hormone release, the preoptic area and hypothalamus have widespread interconnections within the central nervous system. Most of the major projection systems of these regions will be discussed in amphibians, where a more complete picture is available, but one set of hypothalamic connections that is involved in feeding behavior may be unique to ray-finned fishes. This pathway involves a visual input relay through the pretectum, as discussed in Chapter 20. The retina projects to the **parvocellular superficial pretectal nucleus** and to **nucleus corticalis**. In most groups of ray-finned fishes, these two nuclei project to the **posterior pretectal nucleus**, which in turn projects to the inferior lobe of the hypothalamus. In euteleost fishes, the relay from these nuclei to the inferior lobe is through two nuclei—the **intermediate superficial pretectal nucleus** and **nucleus glomerulosus**, which are also located in the pretectal region—rather than through the unitary posterior pretectal nucleus.

The inferior lobe receives a descending input from the telencephalon; in channel catfish, which have an exceptionally well-developed gustatory system, the inferior lobe has been found to project directly to the telencephalon, although it does not appear to do so in other fishes. In percomorph fishes and goldfishes, the inferior lobe as a whole receives afferents from

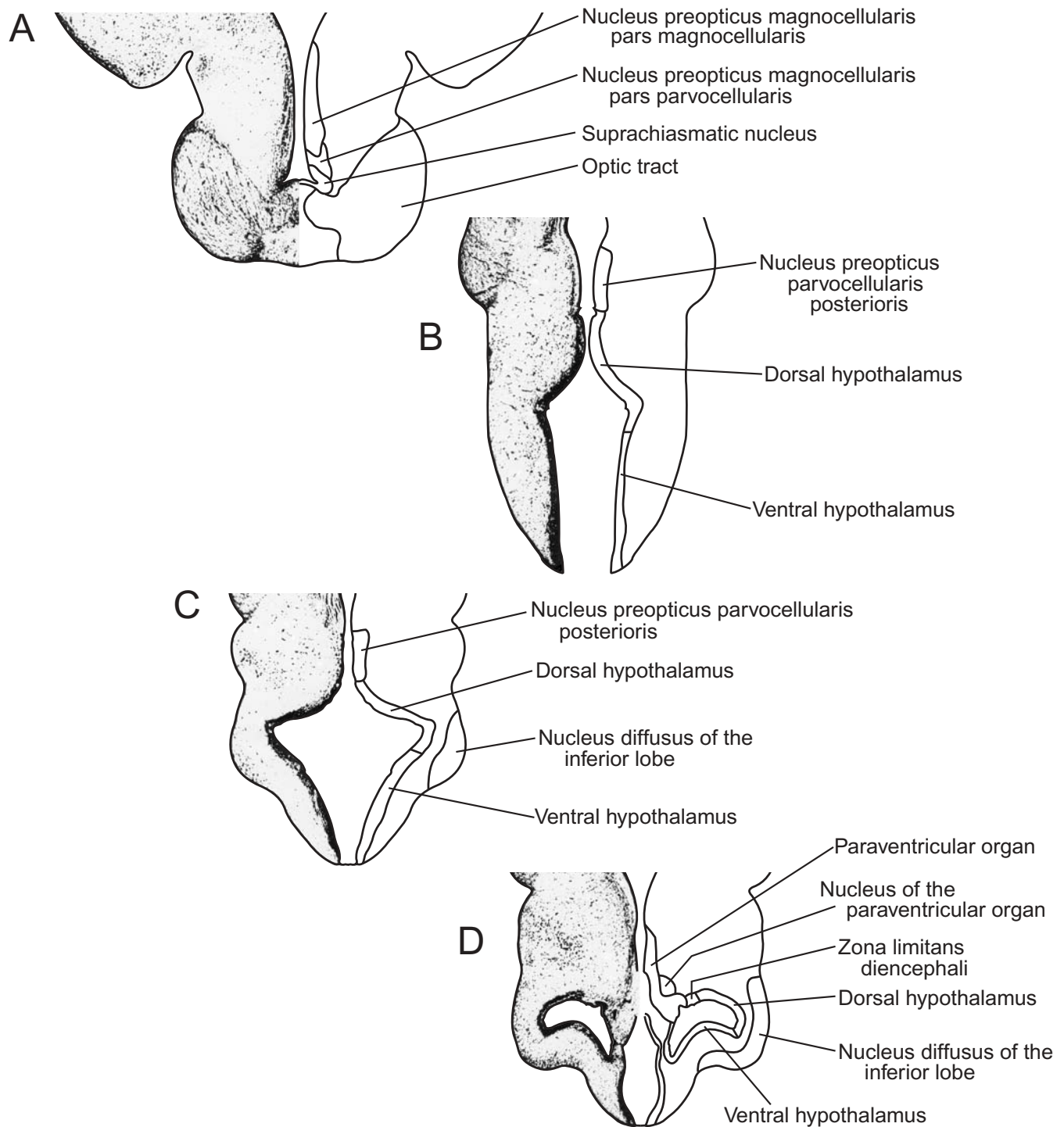


FIGURE 23-5. Transverse hemisections with mirror-image drawings through the diencephalon of a bowfin (*Amia calva*). Section A is most rostral. Adapted from Butler and Northcutt (1992) and used with permission of S Karger AG, Basel.

superior raphe nucleus and the locus coeruleus. In addition, the nucleus centralis of the lobe receives projections from the secondary gustatory nucleus and the preglomerular tertiary gustatory nucleus, as well as from the nucleus lateralis valvulae of the cerebellum. The nucleus diffusus of the inferior lobe

projects to the mammillary bodies and to other subdivisions of the lobe.

Functions of the Preoptic Area and Hypothalamus. Studies involving electrical stimulation of the preoptic area and the

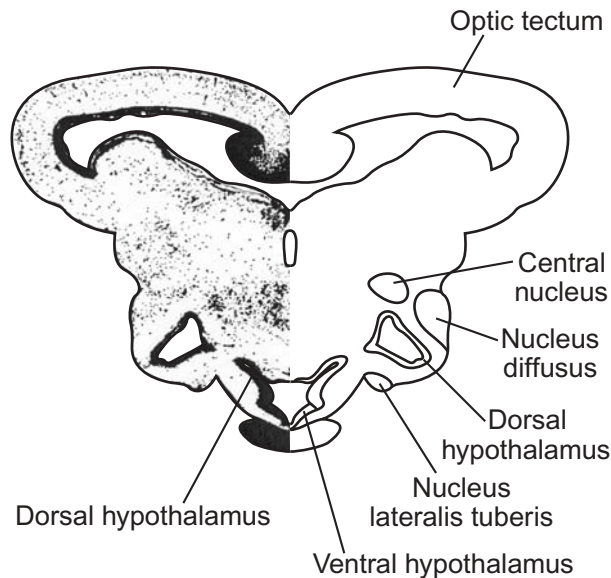


FIGURE 23-6. Transverse hemisection with mirror-image drawing through the caudal diencephalon of a gar (*Lepisosteus osseus*). Adapted from Northcutt and Butler (1980) and used with permission of Elsevier.

hypothalamus shed some light on a number of the behavioral repertoires in which these areas participate. Preoptic area stimulation can result in courtship behaviors and nest building, sperm release, egg release and spawning movements, aggressive behavior, or the display behavior of vertical banding, the latter apparently involving the release of melanocyte stimulating hormone. Stimulation of the dorsomedial part of the hypothalamus results in feeding and agonistic behaviors, vertical banding, sound production, or sperm release. Stimulation of the inferior lobe results in feeding behavior, for which the pretectal afferent pathways were discussed above. Biting attacks, chasing, vertical movements, and circling are also behaviors that have been elicited by inferior lobe stimulation.

Descending projections from the preoptic area to the spinal cord and from the hypothalamus to the medulla may have a role in controlling heart rate in teleosts. Different parts of the hypothalamus appear to have antagonistic roles in increasing or decreasing heart rate in a wide range of vertebrates. In teleosts, stimulation of the preoptic area and the dorsal part of the dorsal hypothalamus results in heart rate decrease, while stimulation of some sites in the inferior lobe results in an increase in the heart rate. Stimulation of other sites in the inferior lobe results in an initial decrease of the heart rate followed by an increase in rate when the stimulation is terminated. Both cardiac regulatory functions and hormonal control systems are correlated with hypothalamic involvement in behavioral displays and reactions as discussed above.

Sarcopterygians

In lungfishes, preoptic and hypothalamic regions are present (Fig. 23-7), but most neurons in these and other regions of the brain are in a periventricular position. The same is true

of these regions in salamanders. In frogs, the preoptic region contains a rostral nucleus, called the **anterior preoptic area**, and two nuclei caudally, a **magnocellular nucleus** and a **suprachiasmatic nucleus**. Within the hypothalamus, two periventricular nuclei are present that comprise the **dorsal hypothalamus** and the **ventral hypothalamus**. A **lateral hypothalamic nucleus** is also present. It is composed of scattered cells and on topographic grounds may be homologous to part or all of the cells in the inferior lobe of the hypothalamus in fishes.

Various nuclei within the preoptic area in amphibians receive multiple inputs, including a major input from the medial pallium. The septum, lateral amygdala, nucleus anterior of the dorsal thalamus, an auditory relay nucleus called the secondary isthmal nucleus, hypothalamus, retina, and epiphysis also project to the preoptic area. The preoptic area projects to the hypothalamus as well as to the striatum and the spinal cord.

The hypothalamus receives a set of afferents similar to those to the preoptic area—from the medial pallium, lateral amygdala, and preoptic area—and additional afferents from the striatum, nucleus anterior and the central nucleus of the dorsal thalamus, the secondary isthmal nucleus, the tegmentum, the secondary visceral nucleus, and the raphe. Efferent targets of hypothalamic projections include the lateral amygdala, part of the subpallium, the preoptic area, nucleus anterior and the posterior nucleus of the dorsal thalamus, the periventricular parts of the pretectum and optic tectum, the torus semicircularis, and the tegmentum. Thus, the preoptic area and hypothalamus comprise a multifaceted interface between the limbic system, sensory systems, and neuroendocrine systems.

THE HYPOTHALAMUS IN AMNIOTES

In this introductory survey, we will not attempt a complete description of the neuronal groups and their various subdivisions in the hypothalamus of amniotes. Instead, we will concentrate on the main nuclei that are common to most mammals, reptiles, and birds. In general, the hypothalamus can be divided roughly into medial and lateral regions, an anterior region, and a posterior region. Many of the nuclei in these regions are shown schematically in Figure 23-8.

The anterior region consists of a cluster of nuclei, some of which are quite small. These include the **anterior nucleus**, the **preoptic area**, which has been subdivided into medial and lateral zones, the **supraoptic nucleus**, the **suprachiasmatic nucleus**, and the **paraventricular nucleus**. The posterior hypothalamus comprises the **mammillary bodies**, which are twin, hemispherical bulges in the floor of the mammalian hypothalamus that bear resemblance (at least in some minds) to human, female breasts. Also in the posterior zone is the **posterior nucleus**, which is located dorsal to the mammillary bodies. The mammillary bodies are subdivided into **medial** and **lateral mammillary nuclei**. In some mammals, an **intermediate mammillary nucleus** is present as well. The main constituents of the lateral region are the **lateral hypothalamic area** (LHA), which is a diffuse region without sharp boundaries. The middle region is sometimes known as the **tuberal region** for the **tuber cinereum**, which means “ash-colored bulge” in Latin, and is a swelling of the floor of the dien-

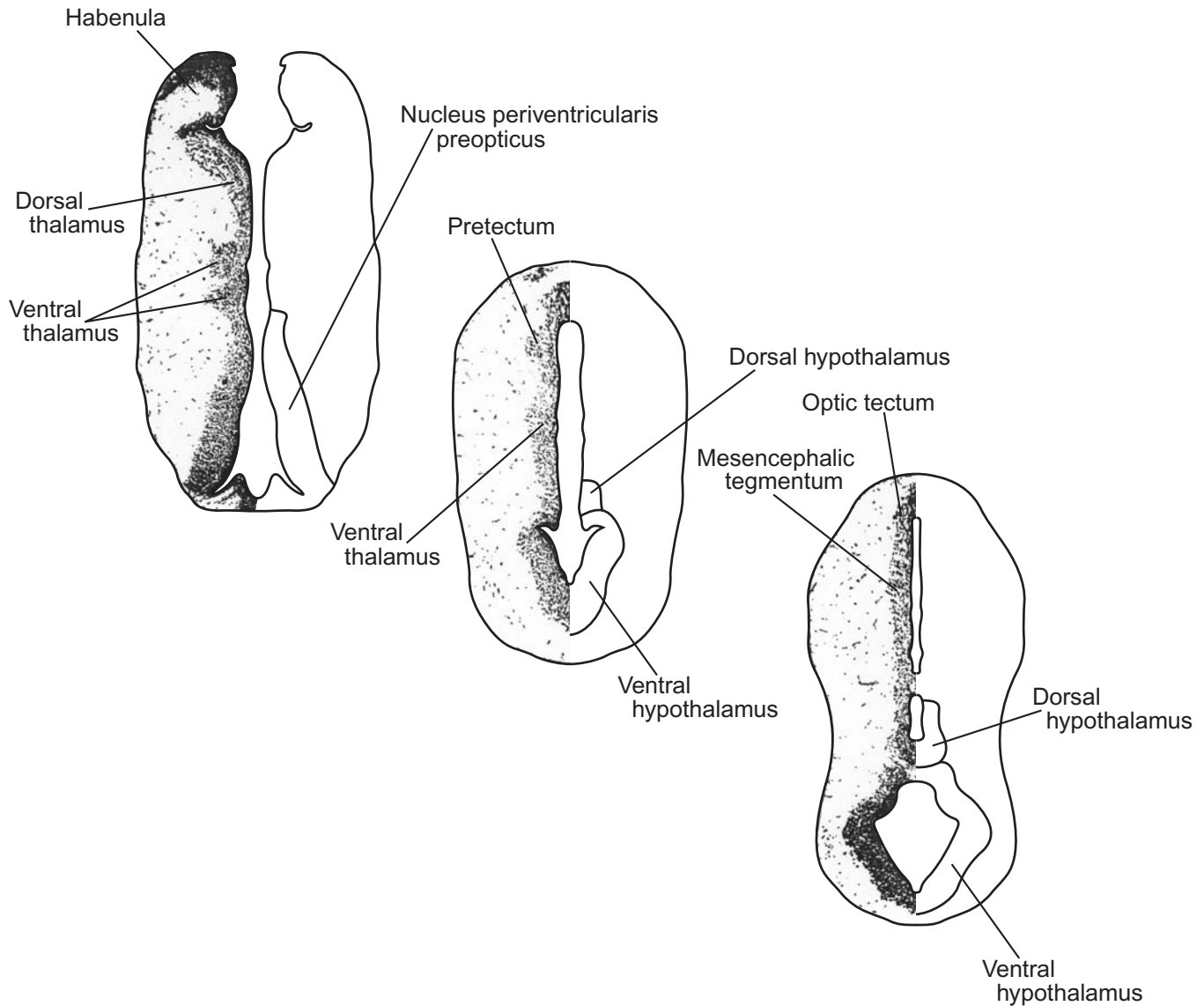


FIGURE 23-7. Transverse hemisections with mirror-image drawings through the diencephalon of a lungfish (*Protopterus annectens*). The hemisection at the upper left is most rostral. Adapted from Northcutt (1977) and used with permission of John Wiley & Sons.

cephalon between the mammillary bodies. The middle or tuberal zone consists of **dorsomedial**, **ventromedial**, and **arcuate nuclei**. Figures 23-9 and 23-10 show some of the preoptic and hypothalamic nuclei in a reptile (a lizard), and a bird (a pigeon).

Connections of the Hypothalamus in Reptiles and Birds

Reptiles. A ventromedial nucleus in the gecko lizard receives afferents from a variety of forebrain sources (the septum, the amygdala, and the dorsal ventricular ridge of the telencephalon) as well as from the habenula and posteroventral nucleus of the dorsal thalamus. Brainstem sources of afferentation include the laterodorsal tegmental nucleus,

the superior raphe nucleus, and the nuclei isthmi. Among the efferents of the ventromedial nucleus is a projection to the centromedial region of the dorsal ventricular ridge. The lateral hypothalamic nucleus receives afferents from such structures as the septal nuclei, dorsal cortex, strio-amygdalar area, the nucleus of the accessory olfactory tract, and the posteroventral nucleus of the thalamus as well as projections from brainstem nuclei, including the nucleus isthmi, the ventral tegmental area, the torus semicircularis, the superior raphe, and the nucleus solitarius. The dorsomedial nucleus also receives input from the septum, dorsal cortex, and posteroventral thalamic nucleus. A suprachiasmatic nucleus in receipt of retinohypothalamic axons is present in the desert iguana as well as a similar pathway to the supraoptic nucleus.

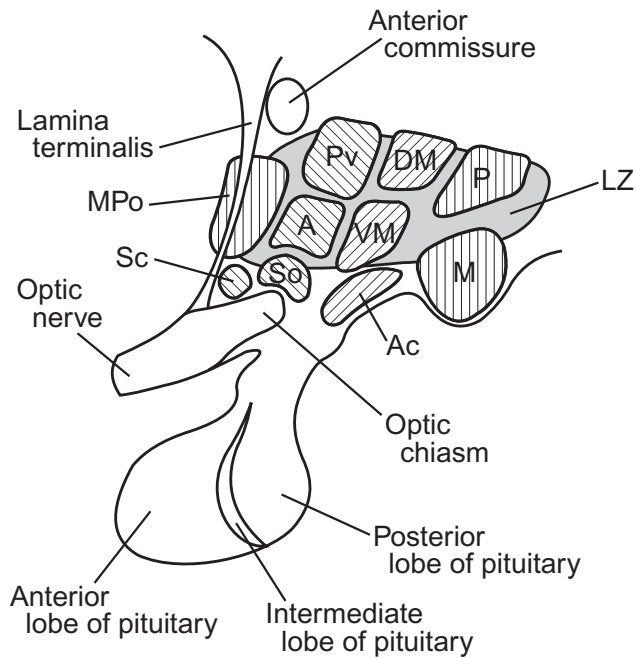


FIGURE 23-8. A schematic representation of major nuclei of the hypothalamus of a mammal. Rostral is to the left. Abbreviations: A, anterior nucleus; Ac, arcuate nucleus; DM, dorsomedial nucleus; LZ, lateral hypothalamic zone; M, mammillary body; MPo, medial preoptic nucleus; P, posterior nucleus; Pv, paraventricular nucleus; Sc, suprachiasmatic nucleus; So, supraoptic nucleus; VM, ventromedial nucleus. Adapted from Haines (2002) and used with permission of Churchill Livingstone.

In snakes, the hypothalamus receives projections from the olfactory system. The major inputs are from the olfactory amygdala to the ventromedial hypothalamus. This pathway includes secondary projections from the nucleus sphericus, which is the recipient of axons from the vomeronasal division of the olfactory system (see Chapter 29). The nucleus sphericus itself sends a minor projection to the lateral hypothalamus. The non-olfactory amygdala, however, projects to the ventromedial hypothalamic nucleus and the periventricular region of the hypothalamus. Similar pathways have been reported in lizards.

Birds. Although the connections of the avian hypothalamus have not been as well studied as those of mammals, the available literature suggests that they have much in common with those of mammals. A **medial forebrain bundle**-like projection connects the hippocampus, septum and parts of the arcopallium to the **lateral hypothalamic area** and preoptic region. The septal nuclei also project to the **ventromedial**, the **periventricular** and **paraventricular nuclei**, and the **mammillary nuclei**. Other sources of input to the hypothalamus are from the **striatum mediale** (formerly called the **lobus parolfactorius**) to the mammillary nuclei; the retina to the **suprachiasmatic nucleus**; and the **parabrachial nuclear complex** to the **anterior preoptic area**, the periventricular nucleus, and the **stratum cellulare internum** and **stratum cellulare externum** of the lateral hypothalamus. These areas,

in turn, are sources of afferents to the dorsal vagal complex of the hindbrain, which is critical for parasympathetic control of the viscera. The periventricular area also receives input from the pineal. Another major input to the hypothalamus in mammals is via the postcommissural division of the **forinx**; this projection, from the hippocampus to the mammillary bodies, is also present in birds.

Among hypothalamic sources of efferents is the **medial preoptic nucleus**, which projects to the hippocampus, septum, and arcopallium. This nucleus is unusual in that it shows a sexual dimorphism, being larger in adult males (see Box 28-1). Moreover, the extent of sexual dimorphism is determined by circulating levels of testosterone that are, in turn, affected by environmental factors, such as seasonal changes in day length, that affect the blood levels of androgens. Thus, the volume of this nucleus changes seasonally. It is permanently affected by castration. By virtue of its connections and relationship with the endocrine system, the medial preoptic nucleus is ideally positioned to play a major role in male sexual behavior. Other hypothalamic efferents are from the mammillary bodies to the septum, hippocampus, arcopallium, and striatum mediale via the medial forebrain bundle.

An interesting feature of the avian hypothalamus is the projection from the stratum cellulare externum (SCE) of the lateral hypothalamus to the **dorsomedial nucleus of the posterior thalamus (DMP)**, which is part of the vocal control circuitry involved in song learning. Because of the paramount role of the hypothalamus in homeostatic mechanisms, the pathway from SCE to DMP may be important for correlation of information about sexual maturation and the effects of circulating hormones involved in growth and reproduction. This function may be of major importance for the development of song learning, which for many species of songbirds is age specific.

Connections of the Hypothalamus in Mammals

The hypothalamus has extensive connections with the diencephalic and mesencephalic components of the limbic system and with the autonomic neuronal groups of the brainstem and spinal cord. Although we discuss them here separately as afferent and efferent, the reader should be aware that many of the connections of the hypothalamus are reciprocal; that is, major pathways of the hypothalamus, such as the medial forebrain bundle or mammillothalamic tract, have axons that travel in both directions.

Afferent Connections. The main afferent connections of the hypothalamus are from the limbic system of the forebrain; that is, the septum, the amygdala, and the hippocampus of the telencephalon and the limbic thalamus, which is the anterior nuclear group in mammals. Because feeding, which depends so much on taste and smell, is central to the functions of the hypothalamus, the olfactory areas of the telencephalon and the gustatory region of the medulla provide inputs to the hypothalamus as well. Olfaction also is important to social and reproductive behaviors, which likewise are important hypothalamic functions. Finally, inputs arrive at the hypothalamus from the midbrain tegmentum, which serves as the contact point between the limbic system and the reticular formation.

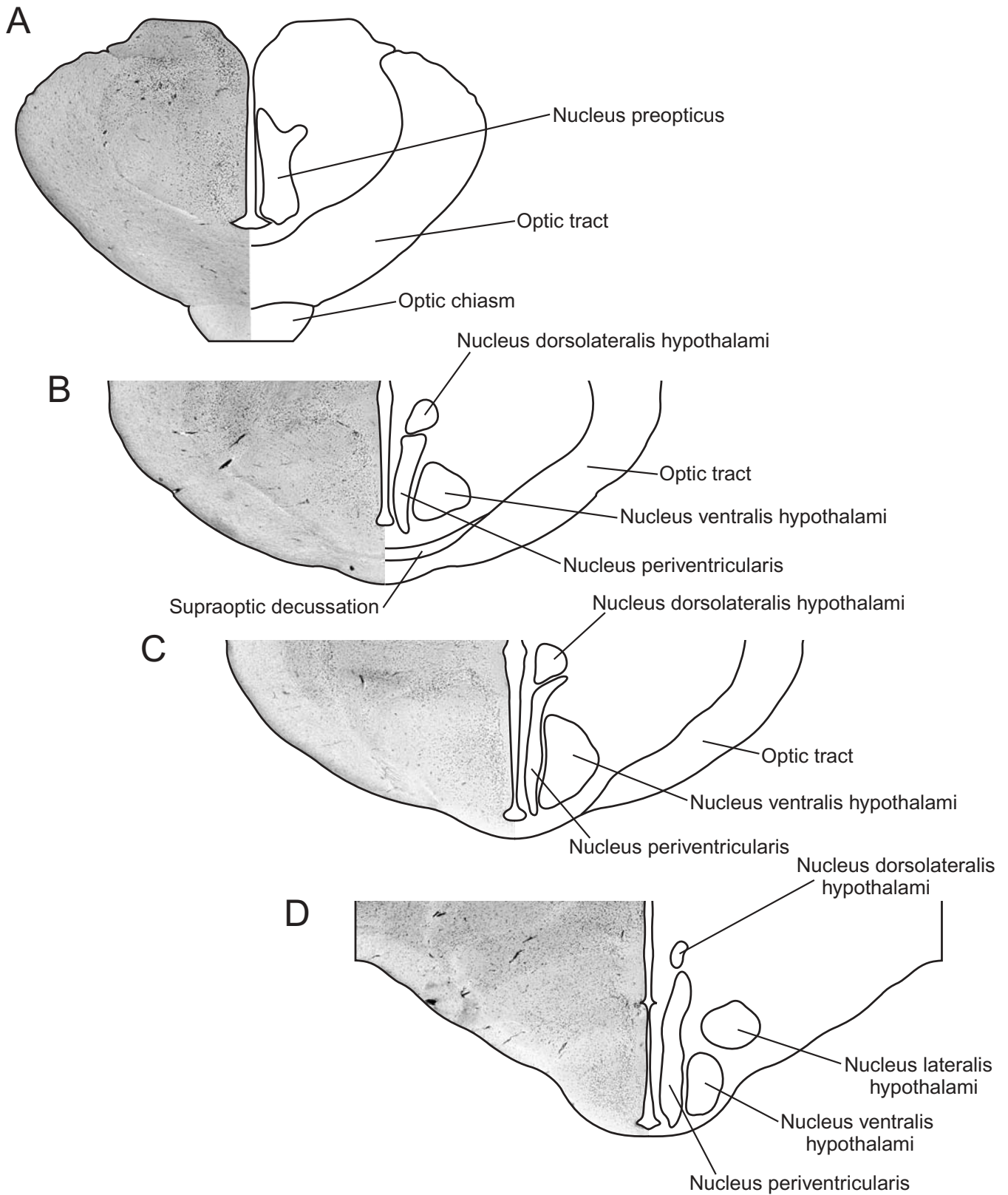


FIGURE 23-9. Transverse hemisections with mirror-image drawings through the hypothalamus, from rostral to caudal (A to D), of a lizard (*Tupinambis nigropunctatus*). Adapted from Cruce (1974).

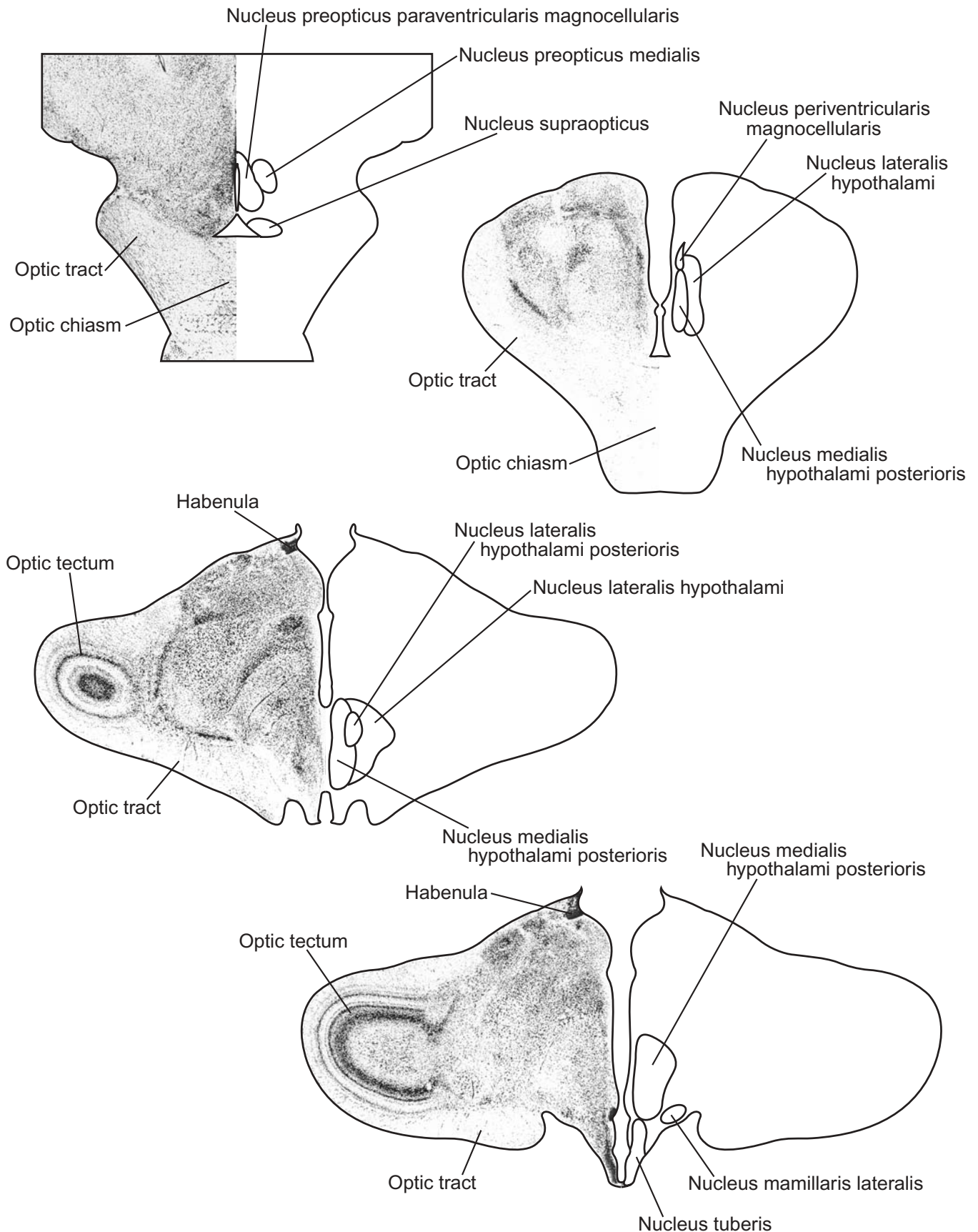


FIGURE 23-10. Transverse hemisections with mirror-image drawings through the diencephalon, from rostral to caudal, of a bird (*Columba livia*). Adapted from Karten and Hodós (1967) and used with permission of The Johns Hopkins University Press.

The following are the main “highways” by which inputs from these regions arrive at the hypothalamus:

- The **medial forebrain bundle**, which contains axons that arise in the olfactory areas of the telencephalon, the septum, the hippocampal formation, and parts of the amygdala and terminate in the lateral hypothalamic area and the lateral preoptic area.
- The **fornix**, which arises in the hippocampal formation and terminates in the medial and lateral mammillary nuclei and the lateral preoptic area.
- The **mammillary peduncle**, which originates in the dorsal and ventral tegmental nuclei of the mesencephalon and terminates in the mammillary body.
- The **dorsal longitudinal fasciculus**, which arises in the periaqueductal gray region of the midbrain and terminates in the periventricular region of the hypothalamus.
- The **ascending serotonergic axons** from the raphe group of nuclei (see Chapter 13), which also travel in the medial forebrain bundle and terminate in the suprachiasmatic and mammillary nuclei as well as in the preoptic area.

Efferent Connections. An important efferent system of the hypothalamus is formed by the pathways that control the sympathetic autonomic neurons of the thoracic and lumbar regions of the spinal cord and the mostly parasympathetic autonomic cranial nerve nuclei of the caudal hindbrain and sacral spinal cord. The autonomic system will be discussed in greater detail later in this chapter. In addition, as we mentioned above, many of the fiber connections of the hypothalamus are reciprocal. Thus a number of the efferent pathways are the same as those of the afferent pathways. These are:

- The **medial forebrain bundle**, which sends axons to the septum, the hippocampal formation, parts of the amygdala, and the raphe group of the reticular formation.
- The **mammillary efferent pathways**, which include the **mammillotegmental tract**, which is the reciprocal pathway from the mammillary body to the dorsal and ventral tegmental nuclei, and the **mammillothalamic tract**, from the mammillary body to the anterior or limbic nucleus of the thalamus.
- The **dorsal longitudinal fasciculus**, which arises in the periventricular region of the hypothalamus and terminates in the periaqueductal gray region of the midbrain.
- The **descending autonomic pathways**, which travel from the paraventricular nucleus and the lateral and posterior hypothalamic areas to the visceromotor cranial nerve nuclei of the medulla, such as the dorsal motor nucleus of the vagus and the nucleus ambiguus, and as far as the intermediolateral column of the spinal cord.
- The **posterior hypophyseal pathways**, which carry the axons of the neurosecretory cells of the supraoptic nucleus and the paraventricular nucleus into the posterior lobe of the pituitary (neurohypophysis) and which are the source of vasopressin and oxytocin.

- The **anterior hypophyseal pathways**, which originate in the medial or tuberal hypothalamus, especially from the arcuate nucleus, and terminate in the median eminence where they stimulate the production of the hypothalamic releasing hormones or factors that travel via the hypophyseal portal system to the adenohypophysis (anterior pituitary) to regulate the synthesis and production of a variety of anterior pituitary hormones.

Functions of the Hypothalamus

The anterior-posterior axis and the medial-lateral axis of the hypothalamus correspond roughly to a functional subdivision of this very complex structure. In a general sense, the anterior and posterior regions of the hypothalamus regulate water balance through their effects on the kidney via the neurohypophysis or posterior pituitary. In addition, these regions are involved in virtually all aspects of reproduction and parental care. These include control of the production and synthesis of the adenohypophyseal (and neurohypophyseal) hormones, the movement of ova in the oviduct, contractions of the muscles of the organs of reproduction, the ejection of fertilized ova, the contractions of the uterus in mammals and viviparous (live bearing) reptiles, and the production of milk in mammals and “crop milk” in pigeons and doves. In addition, the hormones of both the anterior and posterior pituitary are involved in the regulation of the social aspects of reproduction, such as courtship, territorial defense, competition for mates, care of the young, etc. These regions also contain a major pacemaker for biological rhythms, an area that is involved in temperature regulation, and an area that controls the autonomic nervous system. The lateral and medial hypothalamic zones are involved in ingestive behavior (feeding and drinking) as well as aggressive behavior and control of the autonomic nervous system. A number of the functions of the major hypothalamic nuclei and areas are presented in Table 23-4.

The hypothalamus is an important integrating region of the brain; it is a crossroads for influences from the pallial regions of the telencephalon, the limbic system, the reticular formation, sensory systems (especially the gustatory, olfactory, visual, and viscerosensory systems), and control pathways to the endocrine and limbic systems. Some of its nuclear groups, such as the paraventricular and supraoptic nuclei that are in direct control of the contractions of the uterus and the flow of milk in mammals, are essentially motor in the sense that the motor nuclei of the cranial nerves or of the spinal cord are motor; that is, they directly control effector organs. Somewhat less direct control of effectors is exerted by the rest of the neuroendocrine hypothalamus. The majority of hypothalamic neurons, however, are involved in the integration of the many afferent influences and the initiation and maintenance of complex motivations and behaviors that cannot be considered “motor” in any direct sense of that term.

THE AUTONOMIC NERVOUS SYSTEM

At many points in this book we have focused on the somatic motor system, which is the system that moves the skeleton and thus the body. These somatic movements can

TABLE 23-4. Functions of Some of the Major Hypothalamic Nuclei and Areas

Hypothalamic Nucleus or Area	Function
Preoptic area Anterior nucleus	Temperature regulation—cooling of the body
	Reproduction and parental behavior
	Control of the autonomic nervous system
Supraoptic nucleus Paraventricular nucleus	Control of water balance via kidney
	Control of reproductive organs during ovulation and copulation
	Control of milk flow in mammals
	Contraction of uterus in mammals and viviparous reptiles
	Social and parental behavior
	Control of the autonomic nervous system
Posterior nucleus Mammillary body	Temperature regulation—warming of the body
	Control of the autonomic nervous system
Suprachiasmatic nucleus	Pacemaker for biological rhythms
Arcuate nucleus	Control of synthesis and release of anterior pituitary hormones
Lateral hypothalamic area	Feeding behavior
	Drinking behavior
	Aggression
	Control of the autonomic nervous system
Ventromedial nucleus Dorsomedial nucleus	Feeding behavior
	Aggression
	Control of the autonomic nervous system

be reflexive, such as those produced by the cerebellum and vestibular system to maintain posture and muscle tone, or they can be voluntary. We now turn to a motor system that is visceral rather than somatic and that is entirely involuntary; that is, the autonomic nervous system. We have already encountered the autonomic nervous system elsewhere, such as in Chapters 7 and 8.

The autonomic nervous system is composed of three divisions: the **sympathetic division**, the **parasympathetic division**, and the **enteric division**. These sympathetic and parasympathetic divisions work together to provide a smooth

and efficient neural control system for the viscera. The enteric division innervates only the gut and derives its name from the Greek word for intestine. Although the gut does receive some sympathetic and parasympathetic input, the enteric system is a largely autonomous, intrinsic system. It is confined to the smooth muscle wall of the intestines and maintains the peristaltic movements that result in a smooth flow of materials through the gut.

The sympathetic system becomes powerfully activated during times of strenuous exertion, such as sudden escape from a predator, running, fighting, or in contact sports play. During such exertions, the sympathetic division greatly increases heart rate, blood pressure, and respiration as well as stimulates the liver to release extra amounts of glucose into the circulatory system. At the same time, certain other visceral activities are inhibited such as contraction of gut musculature and secretion of digestive enzymes. Because of these dramatic effects, the sympathetic division has the reputation of being an “emergency” system, while the parasympathetic system has the reputation of being the system that operates during nonemergency times. Indeed the word “sympathetic” comes from the Greek word *pathos*, which means “feeling” or “emotion.” Although introductory-level books sometimes state that the parasympathetic system functions to “downregulate” or reduce the functions of an organ and the sympathetic tends to “upregulate” or increase these functions, such statements are overgeneralizations.

Certainly, in the case of the heart, the sympathetic division increases heart rate and the parasympathetic division decreases heart rate. Likewise, the parasympathetic division relaxes certain smooth muscles, such as those of the anal sphincter and the diameter of the bronchus of the lung, while the sympathetic division contracts them. However, the parasympathetic division also stimulates many systems, such the flow of saliva and tears, peristalsis, secretion and blood flow in the gut, secretion of insulin from the pancreas and glucagon from the liver, and erection of the penis and clitoris. Moreover, the sympathetic division increases pupil diameter in response to dim light, whereas the parasympathetic division decreases it in response to bright light. Clearly, neither division falls neatly into a single distinction of upregulation or downregulation. Rather, the two divisions work constantly, even under nonemergency situations, in partnership with each other to maintain a smoothly functioning internal environment.

Some autonomic mechanisms involve a complex interaction between voluntary and involuntary control. One example of this is action of the urinary bladder and sphincter in non-human mammals, in which voluntary urination often is used for scent marking of territory, and in humans, in which involuntary release of urine is socially unacceptable. This control is performed by the sacral component of the parasympathetic nervous system to contract the smooth muscles of the bladder wall, which results in bladder emptying when the bladder is full. The striated muscles of the sphincter are contracted or relaxed by somatic motor neurons of the ventral horn of the spinal cord to result in a controlled, voluntary release of urine. A feedback pathway inhibits the parasympathetic neurons, which has the effect of relaxing the bladder wall at the same time that the ventral horn somatic neurons are excited, thereby

keeping the sphincter muscles contracted to prevent unwanted release of urine.

Autonomic Neurochemistry

Neither the sympathetic nor the parasympathetic division terminates directly on the target organs. Both systems send their efferent axons to ganglia located outside of the central nervous system. The axons from the central nervous system to the ganglia are known as the **preganglionic axons**, and those that leave the ganglion are known as **postganglionic axons**. The neurotransmitter found in the synaptic vesicles of the preganglionic axons of both divisions is **acetylcholine**. In addition, acetylcholine is the neurotransmitter for the postganglionic axons of the parasympathetic division. The postganglionic neurotransmitter of the sympathetic division is **norepinephrine**, except in the adrenal medulla, where it is **epinephrine**. In addition to acetylcholine and norepinephrine, a number of neuropeptides and other neuroactive substances have been found in the autonomic nervous system. These include **vasoactive intestinal peptide**, **enkephalin**, **somatostatin**, **substance P**, **cholecystokinin**, and **nitric oxide**. Some of these substances have sympathetic-like effects and others have parasympathetic-like effects.

Anamniotes

The sympathetic division is located in the thoracic and lumbar levels of the spinal cord and therefore is sometimes referred to as the **thoracolumbar division**. In-coming visceral afferent axons terminate in the **intermediomedial column** of the spinal cord. The outgoing visceral efferent neurons have their cell bodies in the **intermediolateral column**. These sympathetic efferent neurons have relatively short axons, and soon after they leave the spinal cord, they terminate in the sympathetic ganglion (see Chapters 7 and 8). Thus they are preganglionic axons. The postganglionic axons originate in the sympathetic ganglion and terminate in the peripheral organ systems such as the liver, the heart, gut, and glands. Because the sympathetic ganglia are located close to the spinal cord, the postganglionic axons are rather long in order to reach their target organs. The neurotransmitter of the postganglionic sympathetic axon, norepinephrine, is sometimes referred to as noradrenaline; thus the sympathetic postganglionic axons also are known as **noradrenergic axons**.

The visceral motor neurons of the intermediolateral column terminate not only on sympathetic ganglia at their own level of the spinal cord—they also terminate on ganglia that are above or below that level. These ascending and descending connections between adjacent sympathetic ganglia form a longitudinal “chain,” much like beads on a string. This longitudinal chain is known as the **sympathetic chain of ganglia**, or simply as the **sympathetic chain**.

The parasympathetic division differs in many respects from the sympathetic division. First, its neurons are located in the hindbrain and in the sacral levels of the spinal cord. Thus it is sometimes referred to as the **craniosacral division**. Second, its incoming visceral afferent axons terminate in the sensory nuclei of the cranial nerves in the visceral afferent column (see Chapter 10) as well as in the sacral levels of the

spinal cord. The visceral efferent neurons of the parasympathetic division are located in the visceral motor nuclei of the hindbrain, especially that of the **vagus nerve**. Third, the parasympathetic ganglia are located near the target organs rather than close to the central nervous system, which means that the preganglionic axons are rather long and the postganglionic axons are relatively short. Finally, because the neurotransmitter of the postganglionic axon terminals, like that of the preganglionic terminals of both divisions, is acetylcholine, these axons often are referred to as **cholinergic**. Table 23-5 summarizes the main differences between the sympathetic and parasympathetic divisions. Table 23-6 summarizes the target organs of the various components of the autonomic nervous system.

Anamniotes

The autonomic nervous system has not received the same attention by scientists in anamniotes as it has in amniotes, especially mammals and some birds. In general, the autonomic nervous system of anamniotes is not so neatly divided into sympathetic and parasympathetic divisions as it is in amniotes. Moreover, the pattern of dual innervation by both divisions of the autonomic system is not a typical feature of the organs of anamniotes. In general anamniotes, especially nontetrapod anamniotes, have fewer glands in the head than do terrestrial animals because lubrication of the oral cavity and eyes usually is not a problem in the aquatic environment. Jawless vertebrates, for example, have no sympathetic ganglia; axons that are probably sympathetic pass from the spinal cord directly to target organs, such as blood vessels. Jawless vertebrates do have a parasympathetic system that originates in the motor nucleus of the vagus. Cartilaginous fishes, like jawless vertebrates, also lack a well-developed sympathetic system. They do possess sympathetic ganglia, but these are not located in a chain along the side of the spinal cord. Parasympathetic innervation is supplied mainly by the vagus nerve. The stomachs of these animals receive dual sympathetic and parasympathetic innervation.

In ray-finned teleost fishes, a sympathetic chain is present, and dual innervation of additional organs can be observed. A similar pattern can be found in amphibians except that, in these tetrapod anamniotes, the heart is dually innervated by sympathetic and parasympathetic axons. In addition, because amphibians have developed both tear glands and salivary glands, these organs have parasympathetic innervation that originates in the motor nuclei of cranial nerves VII and IX. Some frogs have the sacral component of the parasympathetic division, but this appears lacking in salamanders.

EVOLUTIONARY PERSPECTIVE

The preoptic area and hypothalamus are quite large and well developed in teleosts and cartilaginous fishes, but are relatively small and unelaborated in amphibians. The hypothalamus appears to have undergone an independent expansion in amniotes. Although some variation exists in the structure and organization of these areas, in general the hypothalamus and preoptic area have been fairly conservative in their evolution

TABLE 23-5. Summary of the Autonomic Nervous System

	Sympathetic	Parasympathetic
Location in central nervous system	Thoracic and lumbar spinal cord	Hindbrain and sacral spinal cord
Location of ganglia	Close to spinal cord	Close to target organ
Length of preganglionic axons	Short	Long
Length of postganglionic axons	Long	Short
Preganglionic neurotransmitter	Acetylcholine	Acetylcholine
Postganglionic neurotransmitter	Norepinephrine	Acetylcholine
Effect on heart rate, blood pressure, respiration	Increases	Decreases
Effects on small arterioles	Constriction	Some dilation
Effects on anal sphincter	Constriction	Relaxation
Effects on bladder wall		Contraction
Effects on ciliary muscle and intestinal muscles	Relaxation	Contraction
Effect on dilator pupillae muscle	Contraction	
Effect on constrictor pupillae muscle		Contraction
Effect on muscles that elevate hairs and feathers	Contraction	
Effect on liver	Release glucose	Secretion of bile
Effect on pancreas, stomach, tear glands, and salivary glands		Secretion
Effect on sweat glands and adrenal medulla	Secretion	

TABLE 23-6. Summary of the Major Target Organs of the Autonomic Nervous System

Target Organ	Sympathetic	Parasympathetic
Ciliary muscle, dilator pupillae, constrictor pupillae	Thoracic spinal cord	Nucleus III complex
Salivary glands, tear glands		Nucleus VII and nucleus IX
Adrenal medulla		
Heart, lungs, stomach, liver, pancreas, kidney		Nucleus X
Small intestine	Thoracic and lumbar spinal cord	Nucleus X
Large intestine	Lumbar spinal cord	Nucleus X and sacral cord
Bladder wall and rectal sphincter, gonads, genitals		Sacral cord

in tetrapods. The relationship between the hypothalamus and the endocrine system has undergone some interesting changes, however, in the functions of some of the hormones in different classes of vertebrates. Even though the hormones themselves have remained largely unmodified chemically, their functions in particular classes sometimes have changed. The evolution of the autonomic nervous system has been quite conservative, especially in the tetrapod lineage.

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Part Five

THE FOREBRAIN: TELENCEPHALON

Basal Telencephalon

INTRODUCTION

The basal part of the telencephalon, or subpallium, contains the striatopallidal complexes, the striatal part of the amygdala, several sets of cholinergic neuronal populations, and the septal nuclei. The latter will be discussed in Chapter 30. The striatopallidal complexes are located in the ventrolateral part of the telencephalon and are involved with the control of movements. They are the primary focus of this chapter. In mammals (see Fig. 19-26), the **dorsal striatopallidal complex** is composed of the **caudate nucleus** and **putamen** (which together constitute the **dorsal striatum**) and **globus pallidus (dorsal pallidum)**, while the **ventral striatopallidal complex** is composed of **nucleus accumbens** and the **olfactory tubercle** (which together constitute the **ventral striatum**) and the **ventral pallidum**, the cells of which lie scattered within the rostral part of the substantia innominata, as was discussed in Chapter 19. The term **basal ganglia** varies in its use but can be used for the dorsal striatopallidal complex, for both striatopallidal complexes, or for the latter plus some of the more caudal nuclei involved in their circuitry, such as the substantia nigra. The terms dorsal striatum and/or the ventral striatum are often abbreviated simply to **striatum** when the context is clear.

A number of neurotransmitters and neuromodulators have been identified in the striatopallidal complexes in mammals (see Table 24-1), and similar substances have been identified in some nonmammalian vertebrates in the same ventrolateral region of the telencephalon. These substances are important because of their roles in integrating the various inputs and in transmitting the various outputs of the striatopallidal com-

plexes. They also fortuitously provide markers by which homologues of the mammalian striatopallidal complexes can be identified in nonmammals. Finding a particular neuroactive substance in a particular nucleus or fiber bundle in a nonmammalian vertebrate brain not only helps to identify homologous structures but, as information accumulates, is helping to unravel the functional evolution of this system, particularly the substantial increase in the complexity of motor pathways that occurred within the radiation of land vertebrates.

Of particular note in this regard, both acetylcholinesterase (AChE) and choline acetyltransferase (CHAT) serve as markers of possible dorsal striatal territory, due to the presence of intrinsic cholinergic neurons, particularly in amniotes. Another indication of striatal territory is its substantial innervation by dopamine (DA)-containing and serotonin (5HT)-containing axons that arise from brainstem cell groups. The striatum also contains intrinsic, local circuit interneurons that colocalize somatostatin (SS) and neuropeptide Y (NPY). Most of the SS-NPY interneurons also colocalize neuronal nitric oxide synthase (nNOS) and are thus NADPH-diaphorase positive. Likewise, several subpopulations of GABAergic neurons can be recognized on the basis of colocalization of other neuroactive substances. Within the dorsal striatum, some GABAergic neurons colocalize substance P (SP), while others colocalize enkephalin (ENK). These two subpopulations of GABAergic neurons are Golgi Type I projection neurons that participate in different circuits that control movements.

A third GABAergic population, which colocalizes the neurotensin-related neuropeptide LANT6, is found within both the dorsal striatum and the dorsal pallidum. Within the ventrolateral part of the telencephalon, the absence of SP+ (SP-positive) and ENK+ neuronal cell bodies combined with the presence of

TABLE 24-1. Some of the Histochemical Characteristics of the Dorsal Striatopallidal Complex of Mammals

	Dorsal Striatum	Dorsal Pallidum
Cell Bodies of Intrinsic (Golgi Type II) Neurons	Cholinergic (positive for AChE and CHAT)	
	GABA-LANT6	
	SS-NPY _n NOS	
Cell Bodies of Projection (Golgi Type I) Neurons	GABA-SP	GABA-LANT6
	GABA-ENK	
Substantial Innervation by Afferent Fibers of Particular Transmitter	DA+ fibers from midbrain tegmentum	SP+ woolly fibers from dorsal striatum
	5HT+ fibers from raphe	ENK+ woolly fibers from dorsal striatum

LANT6+ neuronal cell bodies is a good indication of dorsal pallidal territory. Also, the LANT6+ neurons of the dorsal pallidum are projection neurons, whereas those of the striatum are intrinsic, local circuit interneurons. The SP+ and ENK+ fibers of GABAergic dorsal striatal cells that project to the dorsal pallidum have an appearance that has earned them the designation of “woolly fibers,” which are thus an additional indication of dorsal pallidal territory. Identifying these neuron populations and fiber systems in various vertebrate groups, along with dopamine-containing cell populations and other GABAergic cell populations in the brainstem, helps considerably in elucidating the evolution of the system. None of them is exclusive to the dorsal striatopallidal system, but, in combination with location, connections, and other factors, they are of considerable usefulness.

The ventral striatopallidal complex also shares a number of these same features but will be considered somewhat more briefly here. Current information on the ventral striatopallidal complex in hagfishes, lampreys, and cartilaginous and ray-finned fishes is quite limited. It is possible that territory identified as striatal in these taxa may be homologous either to just the dorsal striatum of tetrapods or to the dorsal and ventral striatum combined. The same may be true for pallidal territory.

The key to understanding the striatopallidal system is in noting two basic features of its components. First, many neuronal populations exhibit spontaneous activity, such as the excitatory neurons of most dorsal thalamic nuclei. In the absence of an inhibitory influence, their other inputs result in an increase of their activity, and they thus further stimulate their efferent targets. Second, this system works on the principle of either promoting inhibition or inhibiting inhibition. When inhibition of a cell group is itself inhibited, the cell group is “released” from its constraint and can increase its activity. Thus, whether the net activity of a neural circuit is excitatory or inhibitory depends on the algebraic product of its individual excitatory and inhibitory components.

In addition to striatopallidal forebrain components, the motor-related nuclei of the ventral thalamus (subthalamus) also will be discussed in this chapter. These nuclei are discussed here, rather than in a separate chapter, because their connections are intimately related to the dorsal striatum and pallidum,

particularly in mammals. Nuclei believed to be part of the ventral thalamus, due to their position, have been identified in most groups of vertebrates, but very little information is presently available on their connections in anamniotes. Remember that the nuclei of the ventral thalamus, or subthalamus, are different from the nuclei that constitute the ventral nuclear group, or ventral tier, of the dorsal thalamus (see Chapter 22). Nuclei of the latter group are involved in basal ganglia circuitry, particularly in birds and mammals, but should not be confused with the nuclei of the ventral thalamus. Finally, note that the ascending sensory projections from collothalamus nuclei in the dorsal thalamus to the dorsal striatum in anamniotes were discussed in Chapter 22 and thus will be mentioned only briefly here.

Several groups of large cholinergic neurons that lie within the ventral part of the telencephalon will also be discussed in this chapter. These populations of cells interconnect the limbic-related part of the striatum with the neocortex and other structures. In mammals and perhaps other taxa as well, they are involved in pallial arousal, attention, and related functions.

THE STRIATOPALLIDAL COMPLEXES

Group I

In lampreys, the striatum is present in the medial aspect of the ventral part of the telencephalon and has densely packed cells in its caudal part (Fig. 24-1). GABAergic neurons, some positive for substance P (SP+) and others for enkephalin (ENK+), are present within it, as are dopamine-positive (DA+) fibers that arise from neurons in the posterior tuberculum, and it exhibits a moderate level of AChE. A pallidal region may be present ventrolateral to the striatum, innervated by woolly fibers that arise from the striatal neurons.

In squalomorph sharks, (Fig. 24-2), the striatum lies within the ventrolateral telencephalon in a medial position and is called the **area periventricularis ventrolateralis**. It contains SP+ and ENK+ neurons as well as an innervation by DA+ fibers. It has only low levels of AChE and CHAT, however. A densely packed lamina of cells called the **area superficialis basalis**

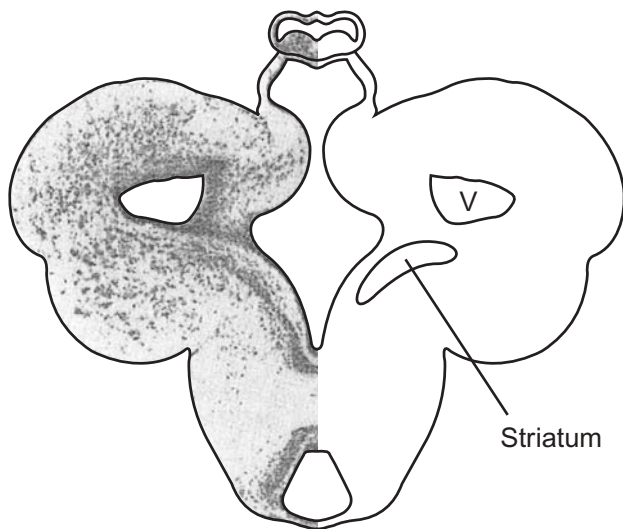


FIGURE 24-1. Transverse hemisection with mirror-image drawing through the telencephalon of a lamprey (*Ichthyomyzon unicuspis*). Adapted from Northcutt and Wicht (1997) and used with permission of S Karger AG, Basel. In this and some other figures, V indicates ventricular space(s).

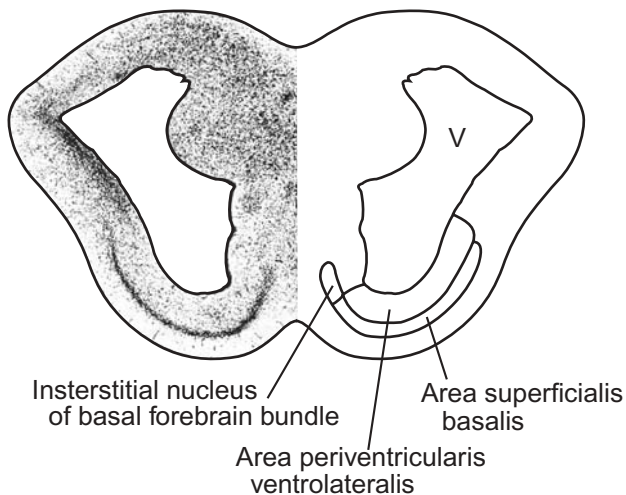


FIGURE 24-2. Transverse hemisection with mirror-image drawing through the telencephalon of a squalomorph shark (*Squalus acanthias*). Adapted from Northcutt et al. (1988) and used with permission of John Wiley & Sons.

lies ventrolateral to the striatum. This area is pallidal, as indicated by its rich innervation by SP+ and ENK+ woolly fibers from the striatal neurons and few DA+ fibers. A smaller medial group of cells, the **interstitial nucleus of the basal forebrain bundle**, may correspond to the ventral pallidum.

The area periventricularis ventrolateralis projects to the dorsal pallidum and to the posterior tuberculum / midbrain tegmental region (Fig. 24-3). Some of the fibers in these projections contain SP, and others contain ENK. The projections of the dorsal pallidum are unknown. The dopaminergic neurons in posterior tubercular-tegmental region in anam-

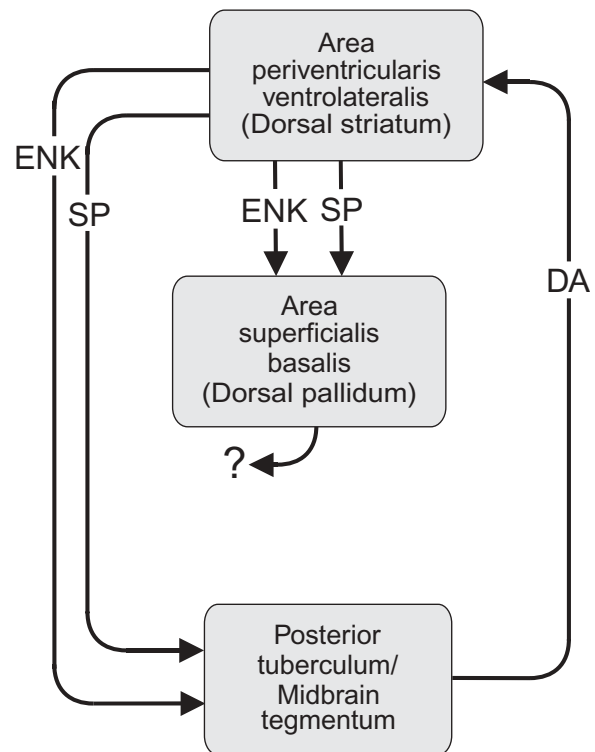


FIGURE 24-3. Connections of the dorsal striatum, area periventricularis ventrolateralis, with the area superficialis basalis (dorsal pallidum) and posterior tuberculum / midbrain tegmentum in sharks. Note that, as for other vertebrates, a serotonergic projection to the dorsal striatum from the raphe is also present but is not included in these diagrams. Abbreviations: DA, dopamine; ENK, enkephalin; SP, substance P. As is also the case for amphibians (Fig. 24-6), the ENK and SP neurons are presumed to colocalize GABA, but this may not have been verified in all cases. The efferents of the dorsal pallidum remain to be determined, as indicated by the question mark.

niotes appear to be homologous to some of the caudal diencephalic (A11) and/or rostral tegmental (A9/A10) dopaminergic neurons in mammals and sauropsids (see Chapter 17). These DA+ neurons project back to area periventricularis ventrolateralis, which also receives a projection of serotonin-containing (5HT+) fibers from the superior raphe.

In nonteleost ray-finned fishes, a number of different groups have been identified in the ventral part of the telencephalon that may be homologous to various striatal and septal forebrain components of amniotes. In the bichir, *Polypterus*, histochemical and connectional evidence suggests that a large periventricular cell group, called the **dorsal nucleus of the ventral telencephalic area (Vd)**, may be the homologue of the dorsal striatum of amniotes (Fig. 24-4). It contains SP+ and ENK+ neuron cell bodies (and the proximal parts of their axons) and 5HT+ fibers. Vd is moderately rich in AChE and CHAT, but, at variance with the general pattern across vertebrates, it receives only a sparse DA+ innervation from cells in the posterior tuberculum. In contrast to the dorsal striatum, a dorsal pallidal region has not been identified in ray-finned fishes. No region that contains either GABA-LANT6 neuron cell

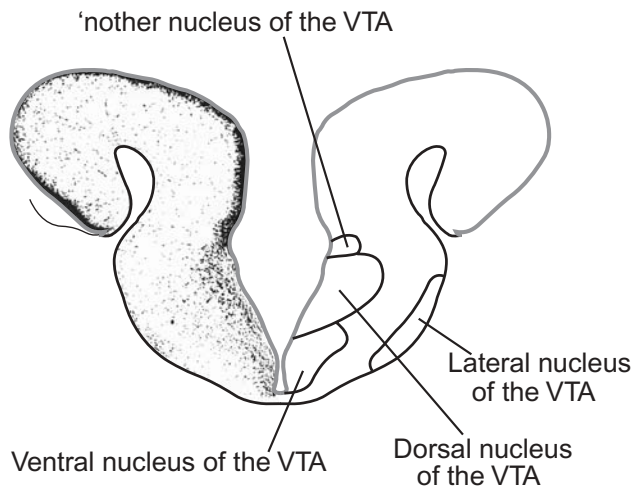


FIGURE 24-4. Transverse hemisection with mirror-image drawing through the telencephalon of a bichir (*Polypterus palmas*). Adapted from Reiner and Northcutt (1992) and used with permission of John Wiley & Sons. VTA, ventral telencephalic area.

bodies and/or SP+ and ENK+ woolly fibers has been found. The striatal region Vd projects to the posterior tuberculum and to part of the midbrain tegmentum, so the functional role of the basal ganglia in ray-finned fishes may be mediated solely by this pathway.

A nucleus dorsal to Vd, whimsically called **'nother nucleus of the ventral telencephalic area (Vn)**, is similar to the caudate-putamen in histochemistry but of uncertain homology due to its location dorsal to Vd. The nucleus ventral to Vd, the **ventral nucleus of the ventral telencephalic area (Vv)**, has reciprocal connections with the limbic part of the pallidum. The ventral nucleus may be homologous as a field to septal nuclei and/or to nucleus accumbens and possibly part of the substantia innominata. Its dorsal part receives ascending gustatory projections. A laterally lying nucleus, known as the **lateral nucleus of the ventral telencephalic area (Vl)**, has connections and histochemistry similar to the medial septal nucleus and the olfactory tubercle of amniotes. It recently has been proposed as a homologue of the nucleus of basalis of Meynert, based in its population of cholinergic neurons (as identified in a trout), which also are present in the medial septal nucleus. Additional studies of connections are needed to clarify the relationships of these nuclei.

Separate striatal and pallidal regions have been identified in both lungfishes and amphibians. In lungfishes [Fig. 24-5(A-B)], the ventral part of the telencephalon can be divided into a medial and a lateral region. Histochemical findings indicate that the medial part of the ventrolateral telencephalon is homologous to the dorsal striatum of amniotes. This region contains SP+ and ENK+ neuron cell bodies and an afferent DA+ innervation and is moderately positive for AChE and CHAT. SP+ fibers project from the striatum to a ventrolateral part of the tegmentum. The cells of this tegmental nucleus project reciprocally to the striatum, supplying its dopaminergic innervation. The striatum is also innervated by serotonin-containing fibers from somewhere in the brainstem—presumably the raphe complex of the reticular formation. A pallidal region lies ven-

trolateral to the striatum. It is low in DA+ fiber innervation but is richly innervated by SP+ and ENK+ woolly fibers from the striatum. It also contains a population of GABA-LANT6+ neuron cell bodies.

In amphibians [Fig. 24-5(C-H)], the dorsal striatum lies in the same ventrolateral position as in lungfishes and contains SP+ and ENK+ neuron cell bodies and 5HT+ and DA+ afferent fibers. The latter fiber system arises from posterior tuberculum/midbrain tegmentum dopaminergic cell groups. Like lungfishes, the dorsal striatum is moderately positive for AChE and CHAT, indicating the presence of a sparse number of intrinsic cholinergic neurons. The dorsal pallidum lies in the basal telencephalon and receives its major input from the dorsal striatum. Its components have previously been identified as part of a cell group called the ventral striatum and the anterior entopeduncular nucleus [Fig. 24-5(D)]. The latter constitutes the caudal part of the dorsal pallidum, as it continues caudally into rostral diencephalic levels.

The true ventral striatum, nucleus accumbens, lies in a ventromedial position through the rostral one-third of the telencephalon. It can be distinguished from the dorsal striatum on the basis of position and due to its denser innervation by SP+ and tyrosine hydroxylase-positive (dopaminergic) fibers. The ventral striatum projects predominantly to the ventral pallidum, which is situated ventral to the dorsal pallidum. As is the case in amniotes, the ventral pallidum can be distinguished from the dorsal pallidum on the basis of a denser innervation by SP+ fibers than ENK+ fibers, the reverse being true for the dorsal pallidum. As is also the case in amniotes, the ventral pallidum receives a substantial noradrenergic input from the locus coeruleus. A further point of similarity with amniotes is that the cholinergic cells of the basal forebrain, which will be discussed below, are scattered within the territories of both the dorsal and ventral pallida.

Both urodele and anuran amphibians share a common pattern of efferent projections from the striatopallidal systems. Many of these projections resemble those seen in amniotes, but some important differences exist as well. Dorsal striatal efferent fibers project to the dorsal pallidum (Fig. 24-6), which gives rise to descending projections, including direct as well as relayed projections to the optic tectum via the pretectum and tegmentum. Pretectal relay of projections from the dorsal pallidum to the optic tectum is not unique to amphibians; similar projections have also been found in amniotes. This input may enhance the ability of the midbrain to mediate orientation behaviors. Efferent projections from the nucleus accumbens-ventral pallidal system only partially overlap those from the dorsal striatopallidal system; this system does not project to the dorsal pallidum or optic tectum, and, unlike the dorsal striatopallidal system, it projects to several more medially lying sites, including the septal region, preoptic area, and ventral hypothalamus.

The basal ganglia circuitry in anamniotes differs from that in amniotes in multiple ways. The heaviest input to the dorsal striatum in frogs arises from the dorsal thalamic nuclei that are in receipt of sensory information from the midbrain tectum. These nuclei are collothalamic sensory nuclei, which in amniotes shift most of their projections to pallial targets. Other inputs are sparser and arise from the dorsal pallidum, amygdala, preoptic area, posterior tuberculum, and superficial

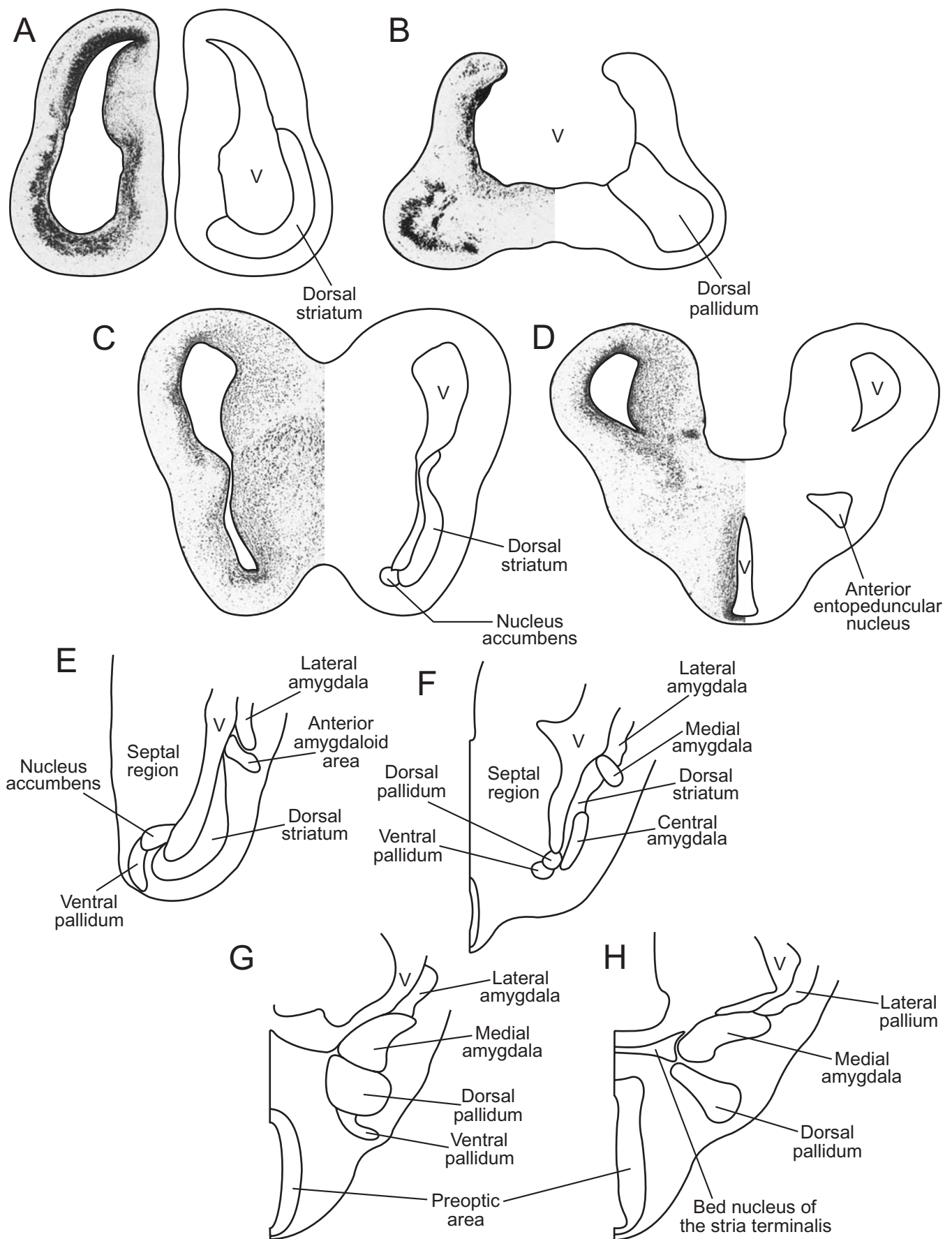


FIGURE 24-5. Transverse hemisections with mirror-image drawings through the telencephalon in (A and B) a lungfish (*Protopterus annectens*) and (C and D) a bullfrog (*Rana catesbeiana*), with the more rostral section to the left in both cases, and a series of drawings (E–H), also in rostral to caudal order, through the striatopallidal region in a bullfrog (*Rana perezi*). Amygdalar components and other landmarks are included in the latter for orientation. Adapted from Reiner and Northcutt (1987), Wilczynski and Northcutt (1983b), and Marin et al. (1998a) respectively. All parts of this figure used with permission of John Wiley & Sons.

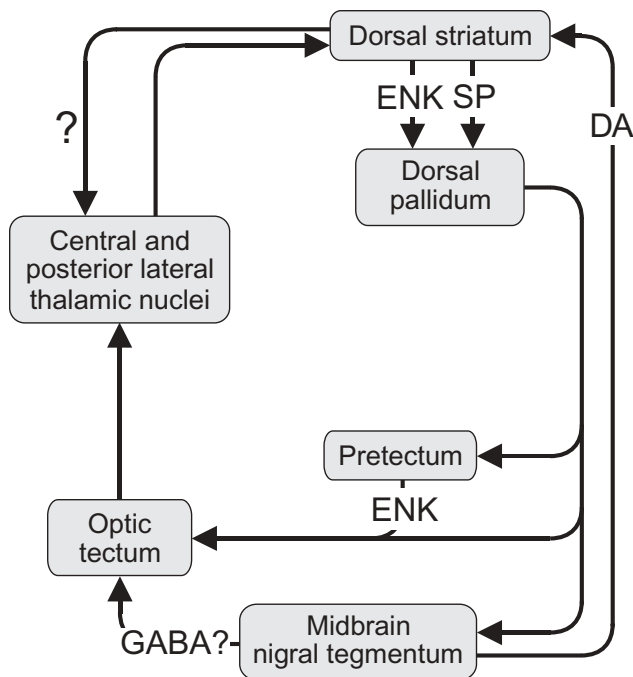


FIGURE 24-6. Some of the connections of the dorsal striatum in amphibians, based on Marin et al. (1998a,b). Most and perhaps all of the direct projections to the optic tectum as well as those relayed through the pretectum and tegmentum arise from the dorsal pallidum, which receives its major input from the dorsal striatum. In contrast to sauropsids, the major thalamic input to the striatum is from the collothalamic, specific sensory nuclei—the central and posterior lateral nuclei—rather than from nonspecific, intralaminar-like nuclei. The striatum may project back to these nuclei directly. The question mark indicates the uncertainty of this projection. Alternatively, the pallidum may give rise to these thalamic projections. Not included here are projections from the dorsal striatum to the posterior tubercular / tegmental region, which are a shared feature of most vertebrate groups. Abbreviations for neurotransmitters are as in Figure 24-3.

isthmal reticular formation. Also, dorsal thalamic projections to the dorsal striatum from nonspecific, intralaminar-like nuclei have not been identified in any anamniote, and input from pallial areas of the telencephalon is very meager to nonexistent. In amphibians, collothalamic sensory projections to the dorsal striatum and motor outputs via the dorsal pallidum to the midbrain roof predominate. This situation contrasts markedly with the shift to nonspecific sensory inputs to the striatum and motor outputs via the dorsal pallidum-ventral nuclear group-pallial circuits that evolved in the amniote line, as discussed below.

Group IIA

In the enlarged and elaborate telencephalon of hagfishes, the identification of a striatum is uncertain. The current candidate is a cell group called striatum that lies deep to the pallial areas in the central-basal part of the telencephalon but rostro-lateral (rather than ventrolateral as in other vertebrates) to the

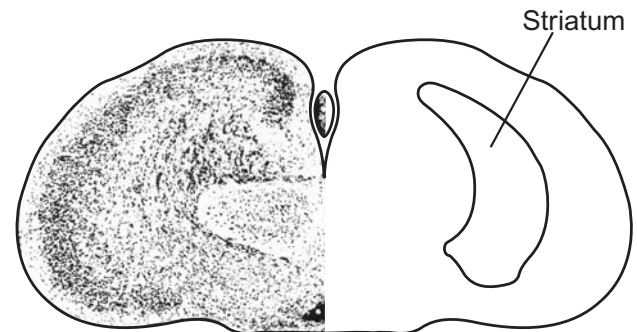


FIGURE 24-7. Transverse hemisection with mirror-image drawing through the telencephalon in a hagfish (*Eptatretus stouti*). Adapted from Wicht and Northcutt (1992) and used with permission of S. Karger AG, Basel.

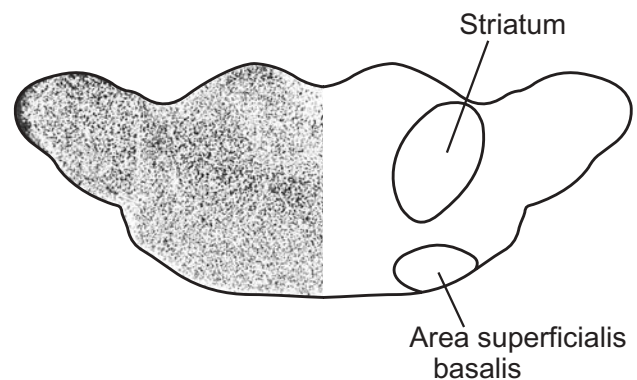


FIGURE 24-8. Transverse hemisection with mirror-image drawing through the telencephalon of a skate (*Raja eglanteria*). Nissl photomicrograph courtesy of R. Glenn Northcutt.

lateral ventricle (Fig. 24-7). This cell group includes SP+ and ENK+ perikarya, and its neuropil is moderately positive for AChE. It receives DA+ projections from the posterior tuberculum, and fibers of a basal forebrain bundle arise and/or terminate within it. No information is available as to whether a pallidal region exists.

In galeomorph sharks, skates, and rays, a region in the ventral part of the telencephalon named nucleus superficialis basalis may be the homologue of nucleus accumbens and possibly also the olfactory tubercle of mammals, rather than being pallidal as is the lamina of cells with the same name in squalomorph sharks. A more diffuse mass of cells dorsal to this lamina has been identified as dorsal striatum and corresponds to the cell group named area periventricularis ventrolateralis in squalomorph sharks, the probable homologue of the caudate-putamen of mammals. In skates (Fig. 24-8), but not in sharks, the striatum (area periventricularis ventrolateralis) has been found to receive ascending visual projections relayed from the midbrain roof through the dorsal thalamus and may receive other sensory input as well. Dopamine-containing fibers have been found in the striatum and nucleus superficialis basalis in rays. Somatostatin- and neuropeptide Y-containing cell bodies are also present in the basal telencephalon in sharks.

In teleost fishes (Fig. 24-9), hypertrophy of the telencephalon combined with the developmental process of eversion (see Chapter 3) has made topological comparisons difficult. Histochemical and connectional data are not yet adequate to completely clarify this situation. Three cell groups in the ventral telencephalon are present that correspond to cell groups in the bichir *Polypterus*: the dorsal (Vd), ventral (Vv), and lateral (Vl) nuclei of the ventral telencephalic area.

The dorsal nucleus of the ventral telencephalic area (Vd) in all ray-finned fishes is a good candidate for a homologue of

the dorsal striatum of other vertebrates. In teleosts, Vd contains DA+ and 5HT+ fibers as well as SP+ and ENK+ perikarya. The neuropil is also moderately positive for AChE and CHAT. Also, GABAergic striatal neurons (probably either SP+ or ENK+ colocalizing) project to the posterior tuberculum. An additional nucleus present in teleosts (not shown in Fig. 24-9), called the **central nucleus of the ventral telencephalic area (Vc)**, also has been tentatively identified as part of the striatum, since it also contains SP+ perikarya. No cell group homologous to the dorsal pallidum (globus pallidus) has been identified, however. As for Group I ray-finned fishes, other ventral telencephalic components can be homologized tentatively to nonstriatopallidal subpallial structures in amniotes. The ventral nucleus (Vv) may be homologous as a field to the septal nuclei, nucleus accumbens, and perhaps part of the substantia innominata. It has catecholamine-, 5HT-, SP-, and ENK-containing fibers. The lateral nucleus (Vl) is striatal-like in that it contains cholinergic neurons, somatostatin-containing neurons, and neuropeptide Y-containing neurons. It resembles the olfactory tubercle of mammals in that it has an olfactory input. It alternatively has been proposed as a homologue of the nucleus basalis of Meynert.

Group IIB

With the invasion of the land, changes occurred in the motor system to accommodate a new, more expanded set of movements. The striatal motor system governs the movements of the trunk and limbs. Much of its output is inhibitory in order to prevent all but the desired movements. As we discussed in Chapter 19, the striatopallidal complexes have two divisions, which are particularly well developed in amniotes. In mammals, the dorsal striatopallidal complex (Fig. 24-10) lies deep to the white matter of the overlying cortex and is bordered medially by the fibers of the internal capsule. The dorsal

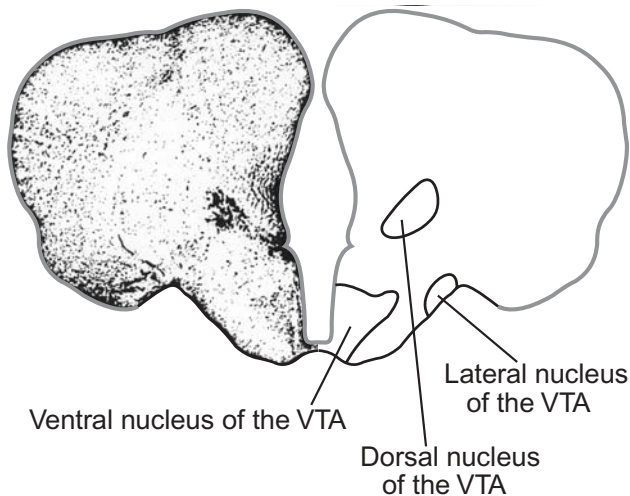


FIGURE 24-9. Transverse hemisection with mirror-image drawing through the telencephalon of a teleost (*Lepomis cyanellus*). Adapted from Northcutt and Davis (1983). VTA, ventral telencephalic area. Note that the everted ventricular surface is shown in gray. Used with permission of the University of Michigan Press.

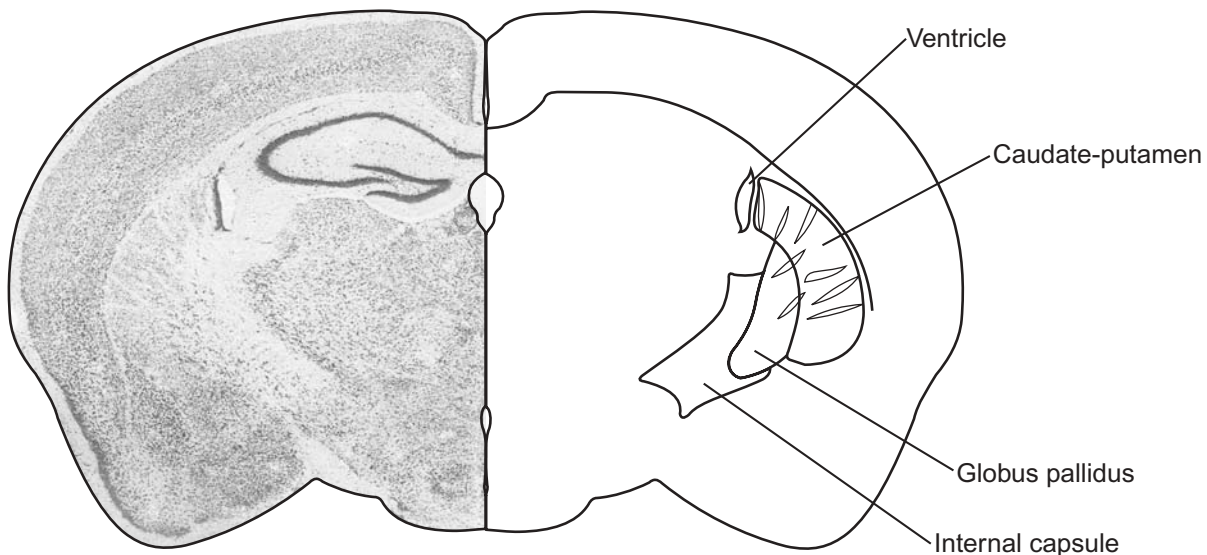


FIGURE 24-10. Transverse hemisection with mirror-image drawing through the telencephalon of a mouse (*Mus musculus*). Bundles of fibers are shown penetrating the caudate-putamen and globus pallidus on their way to or from the internal capsule. Adapted from Slotnick and Leonard (1975).

complex contains the dorsal striatum (caudate nucleus and putamen) and the dorsal pallidum (globus pallidus). In mammals, the globus pallidus comprises two segments—a lateral, or external, segment, and a medial, or internal, segment. The ventral complex contains the ventral striatum (olfactory tubercle and nucleus accumbens) and the ventral pallidum (a rostral part of the substantia innominata). These structures lie rostral to the level shown in Figure 24-10. For reference, Table 19-7 presents a summary of subpallial nomenclature in mammals, and Table 19-1 shows terminology for birds.

The striatopallidal complexes are involved with circuits that interconnect pallial premotor and motor areas with the dorsal thalamus and with the subthalamus (i.e., the ventral thalamus), mesencephalic dopaminergic cell groups [(substantia nigra (A9), ventral tegmental area (A10), and retrorubral field (A8)], and other related nuclei. The connections of the striatum with ventral thalamic nuclei are best understood in mammals, but some information on this circuit is also available for nonmammalian amniotes. We will briefly digress to cover the ventral thalamus in amniotes here and then return to a comparative view of the striatopallidal systems.

The Ventral Thalamus. In mammals, three ventral thalamic nuclei lie medial to the globus pallidus (Fig. 24-11). One of these nuclei now is known as the **subthalamus nucleus** but originally was called the corpus Luysii (meaning the “body, or nucleus, of Luys”). It was named such by August Forel in 1877, a Swiss neurologist, in recognition of its description by Jules Bernard Luys, an eminent French neurologist of the 19th century. The subthalamus nucleus receives GABA-LANT6+ inhibitory projections from the external part of the globus pallidus and in turn projects to the internal part of the globus pallidus with an excitatory, glutamatergic input. As we will discuss

below, this nucleus is a key part of a circuit that normally inhibits the production of unwanted movements. Its other connections include reciprocal connections with substantia nigra pars reticulata and inputs from the neocortex, substantia nigra pars compacta, and the pedunculopontine nucleus.

The second ventral thalamic nucleus in this region is the **zona incerta**, which lies dorsal to the subthalamus nucleus. It links motor cortex with efferent targets that include other parts of neocortex and the superior colliculus, pretectum, and pons.

The third nucleus, which is called the **nucleus of field H of Forel**, is composed of cells scattered among fiber tracts and constitutes the major component of the **subthalamus reticular nucleus**. It lies at the level of the mesodiencephalic junctional region, immediately rostral to the red nucleus and ventrolateral to the ventral tegmental area. In discussions of the ventral thalamus, the terminology of the **fields of Forel** is frequently encountered. The fields are named for their discoverer, August Forel, who reported them in 1877 along with his description of the subthalamus nucleus. Forel used the designations H, H₁, and H₂ for these fields. The letter H stands for *Haubenregion*, which is the German word for tegmentum. At present, this terminology is more of historical interest than of practical application.

Specific portions of fiber tracts, most of which arise in the globus pallidus and loop through the subthalamus region, are also named (Fig. 24-11). The **subthalamus fasciculus** consists of fibers that reciprocally connect the globus pallidus with the subthalamus nucleus. Fibers of the **lenticular fasciculus**, which is also called field H₂ of Forel, arise from the internal part of the globus pallidus and pass between the zona incerta and the subthalamus nucleus. Fibers of the **ansa lenticularis** arise from the internal part of the globus pallidus and pass ventral and then medial to the subthalamus nucleus. The latter

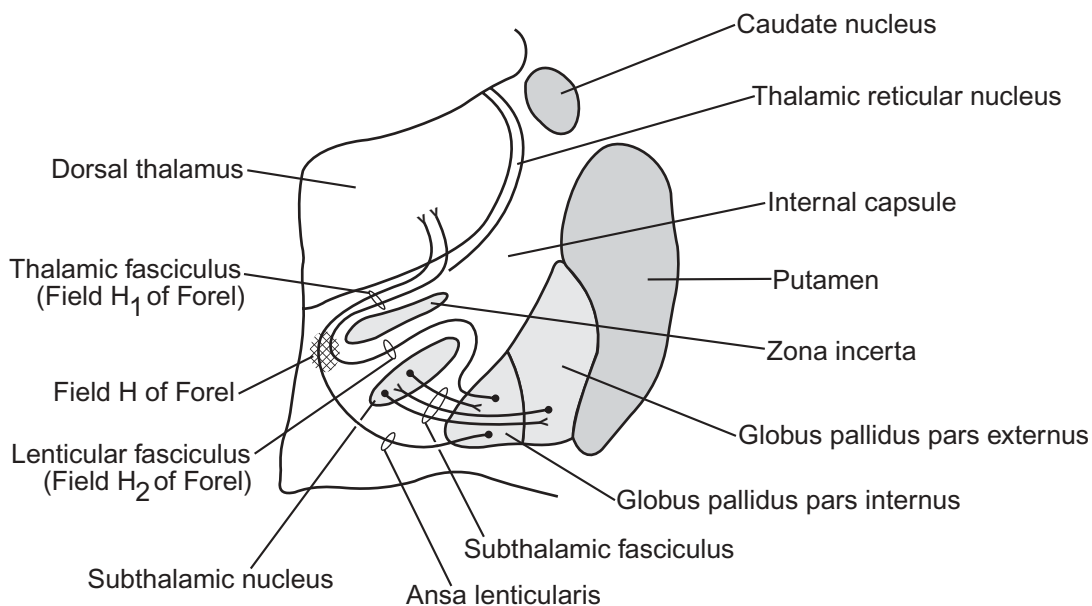


FIGURE 24-11. Semischematic drawing of a transverse hemisection through the right diencephalon and striatopallidal region of a primate (*Homo sapiens*). Dorsal is toward the top and lateral toward the right.

two fascicles join and enter the **thalamic fasciculus**, which is also called field H₁ of Forel, to project to the ventral nuclear group of the dorsal thalamus.

The subthalamic nucleus is the main component of the ventral thalamus that participates in basal ganglia circuitry (Fig. 24-12). As noted above, its major relationship with the basal ganglia comprises an inhibitory input from the GABA-LANT6 neurons of the external segment of the globus pallidus and a glutamatergic, excitatory projection from it to the internal segment of the globus pallidus. We will discuss the significance of these connections below in conjunction with a circuit called the indirect loop. This circuit is also augmented by the connections of the subthalamic nucleus with the substantia nigra, pars reticulata. The subthalamic nucleus receives additional inputs from the neocortex, substantia nigra pars compacta, and nucleus pedunculopontinus, which further affect its influence on the internal segment of the globus pallidus.

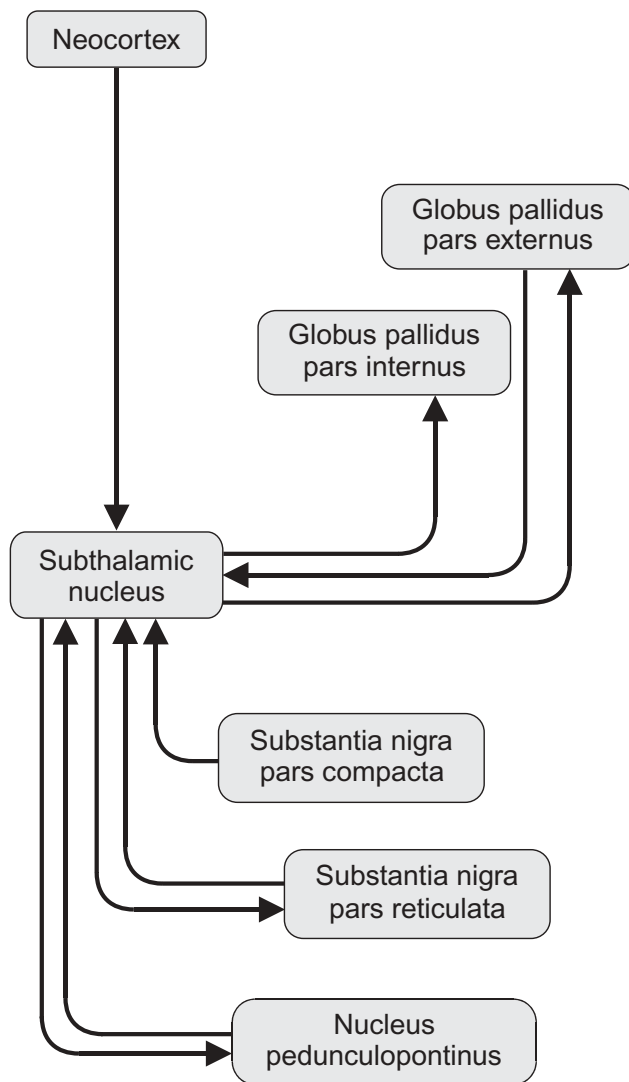


FIGURE 24-12. Some connections of the subthalamic nucleus in mammals.

A homologue of the subthalamic nucleus has been identified in sauropsids. Similarities with the mammalian subthalamic nucleus include its glutamatergic neurons, projection to the globus pallidus, and location. In birds, this nucleus was previously called the anterior nucleus of the ansa lenticularis (ALa), but it has been renamed the subthalamic nucleus. In reptiles, a nucleus called the **anterior entopeduncular nucleus (ENa)** has similarly been identified as the homologue of the subthalamic nucleus, based on its location and its glutamatergic cell population. A possible problem with nomenclature may exist, however; an apparently different, GABAergic cell population in the telencephalo-diencephalic transition area that is also called ENa may be homologous to part of the globus pallidus. It receives projections from the dorsal striatum and projects to the region of the putatively intralaminar-like region in the rostral part of the dorsal thalamus.

The Mammalian Striatopallidal Complexes. The striatum is not homogeneous in its structure. For example, different parts of the dorsal striatum receive inputs from associational, sensorimotor, and limbic-related regions of neocortex. These inputs are partially overlapping in varying degrees. The dorsal striatum also has a compartmental organization in that it contains a mosaic of **patches** within a **matrix**, as first described in rats. The patches are regions of high μ -opiate receptor binding within the matrix of lower receptor binding. Neurons within the patches receive input from neocortical areas and have reciprocal connections with the ventral part of the A9 (substantia nigra) dopaminergic cells in the tegmentum. Neurons within the matrix receive input from neocortical areas and also from dopaminergic cells in the intermediate part of A9. They project to GABAergic neurons in the pars reticulata of the substantia nigra. A similar compartmental organization identified in cats and monkeys has been referred to as a **striosome/matrix** organization. Discrete zones within the matrix that receive somatotopically organized projections from sensory and motor cortices have been identified as **matrixes**. Some of the neurons within the face and arm region of the putamen respond to visual as well as tactile stimuli and thus provide a map of space for these two modalities within the dorsal striatum.

Nucleus accumbens has two major parts: a **core** that is continuous cytoarchitectonically with the caudate-putamen and a **shell** region around the core. A rostral pole region is also recognized as a separate entity. While the patch/matrix organization in the dorsal striatum is bicompartamental, the connectivity and neurochemical patterns within different areas of nucleus accumbens suggest a much more complex, multicompartamental organization.

The dorsal striatopallidal complex is involved in the regulation of voluntary movements for the body. It contains a complex array of neuronal elements and connections. The connections of the dorsal striatum, or caudate-putamen (Fig. 24-13), include a major input from the intralaminar nuclei (particularly the parafascicular nucleus and, in primates, the central lateral nucleus; see Table 22-1) and a lesser input from two nuclei of the ventral nuclear group, nuclei ventralis anterior (VA) and ventralis lateralis (VL). It also receives a major input from neocortex. These inputs are all glutamatergic, excitatory inputs. An additional major input is from the dopaminergic

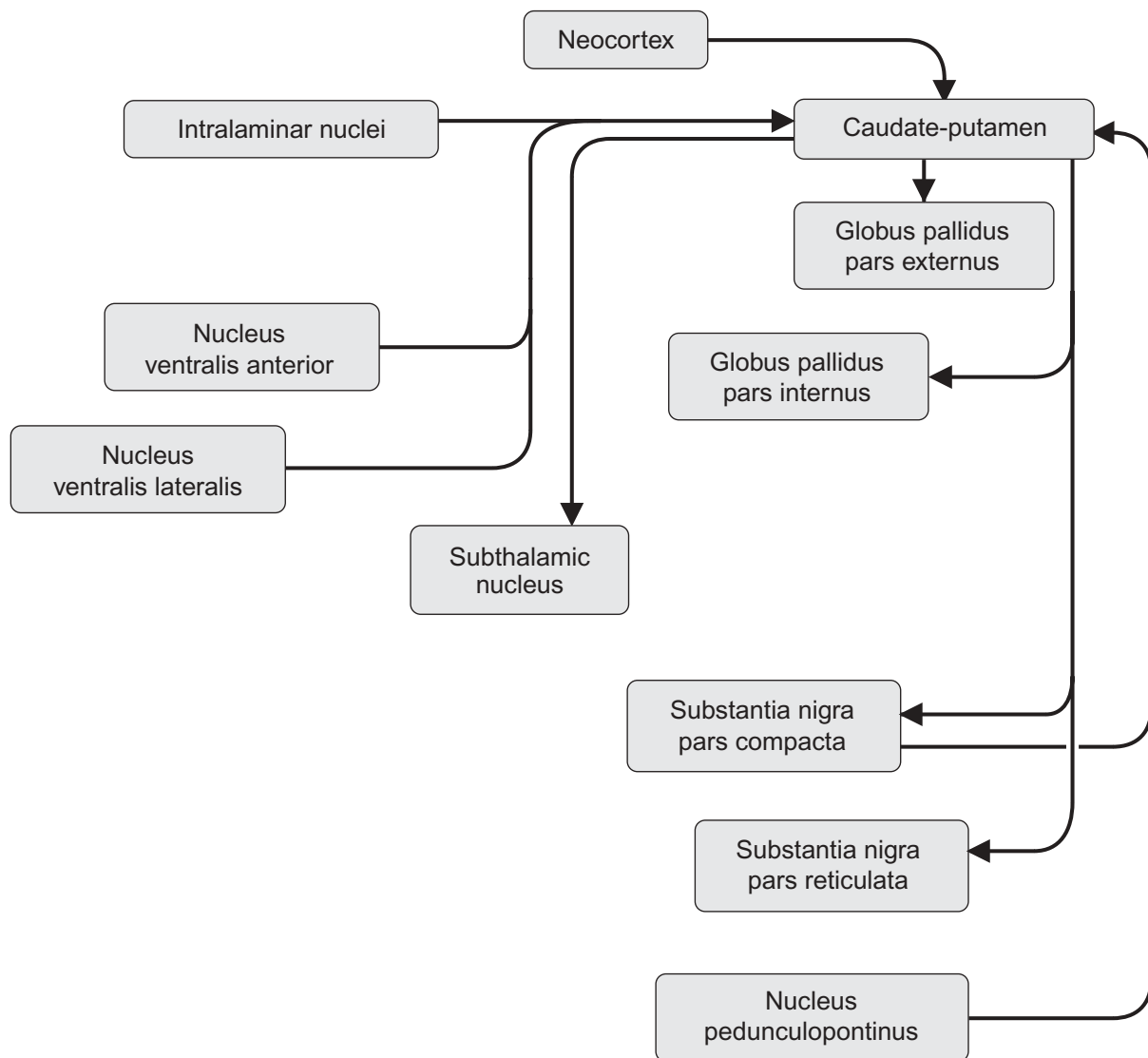


FIGURE 24-13. Some connections of the dorsal striatum in mammals. Not included here are collateral, afferent projections to the dorsal striatum that arise from collothamic nuclei.

neurons of the substantia nigra pars compacta (SNc) and the serotonergic neurons of the raphe. Other inputs include that from the cholinergic neurons of nucleus pedunculopontinus and sensory inputs from collothamic nuclei of the dorsal thalamus. The major efferent target of the dorsal striatum is the globus pallidus—both external and internal segments. It also projects to the subthalamic nucleus and both parts of the substantia nigra.

The dorsal pallidum, the globus pallidus, likewise has a complex array of connections (Fig. 24-14). Its external segment, GPe, receives a major inhibitory input from the GABA-ENK+ neurons of the caudate-putamen and a lesser, excitatory input from the subthalamic nucleus. Its two major efferent targets are the internal segment, GPi, and the subthalamic nucleus. GPi receives a major afferent input from GPe and other inputs from a number of nuclei, including the GABA-SP+ neurons of the caudate-putamen, as well as from the subthala-

mic nucleus and SNc. It projects reciprocally to GPe and gives rise to a major projection to the dorsal thalamic nuclei VA and VL. It also projects to the intralaminar nuclei.

A minor projection of the globus pallidus is also of note for comparison with reptiles and birds. The latter have a robust projection system from the globus pallidus to the pretectum, which then projects to the optic tectum, relaying the pallidal input to the midbrain roof as will be discussed below (and see Chapter 20). In mammals, the projection is small but apparently present. The globus pallidus projects to the posterior pretectal nucleus, which in turn projects to the superior colliculus.

Two major circuits of the dorsal striatopallidal complex have been identified that function in concert to facilitate or inhibit movements. These circuits are called the **direct loop** and the **indirect loop**. During the waking state, these loops might be compared to driving an automobile with one foot on

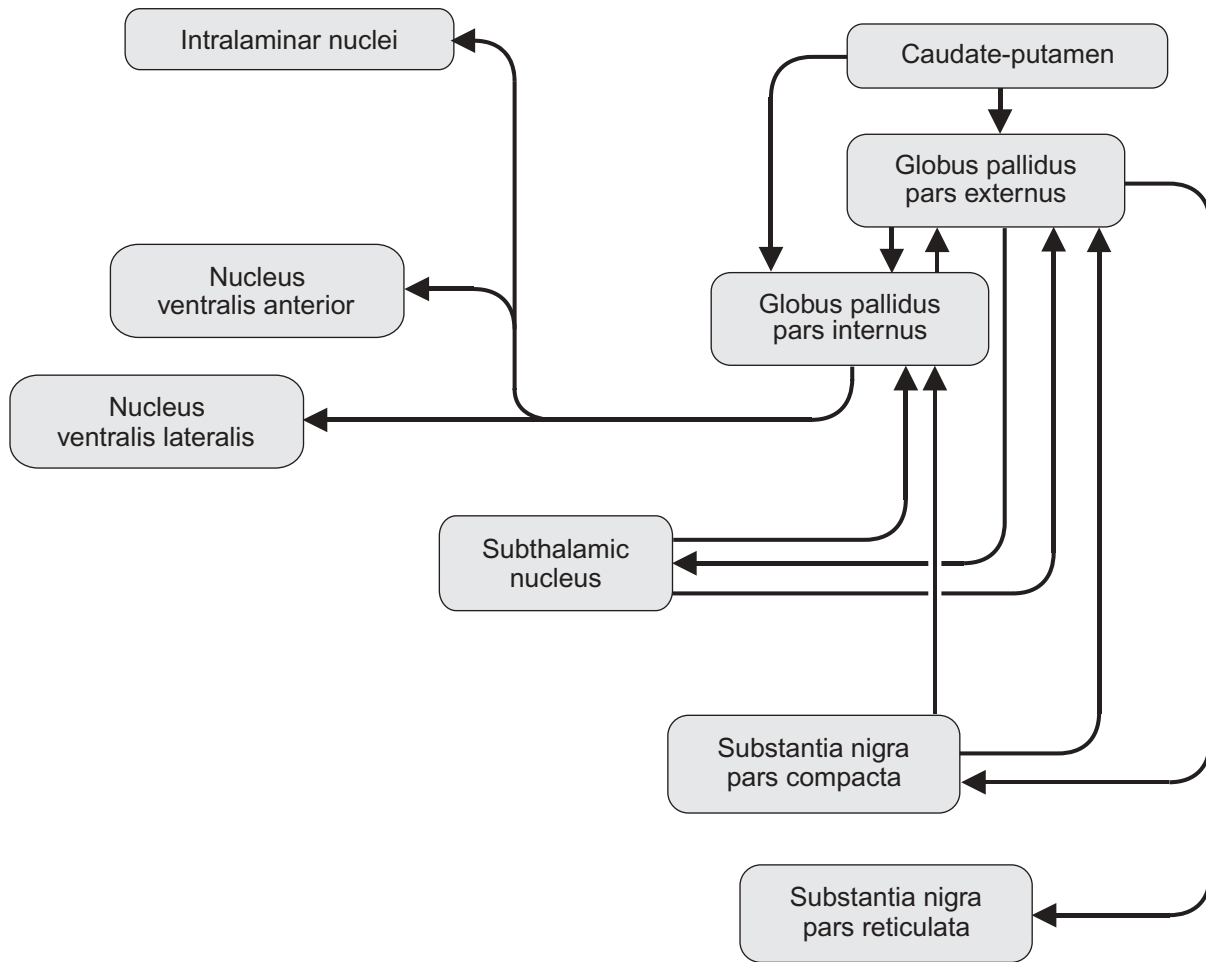


FIGURE 24-14. Some connections of the dorsal pallidum in mammals.

the accelerator (the direct loop) and one foot on the brake (the indirect loop) at the same time. For an automobile, this practice eventually damages the brakes, but for the nervous system this type of balance normally allows both the initiation of voluntary movements and the ability to be at rest. Damage to various components of these loops results in either the occurrence of involuntary movements (such as writhing or flinging movements of the extremities and/or tremors) during the waking state and/or the inability to move when one desires to do so, even if the muscles are not paralyzed.

The direct loop (Fig. 24-15) facilitates movement. Its primary circuit involves VA/VL, the neocortex, the caudate-putamen, and the internal segment of the globus pallidus. Two of the synapses in this circuit are excitatory, and two are inhibitory, resulting in a net excitatory affect. For example, assume that each of the excitatory and inhibitory influences in Figure 24-15 has a value of one and that there is also some level of spontaneous activity in each of the structures. If we multiply these influences, the product is +1 $[(+1)(+1)(-1)(-1) = +1]$, indicating a net excitation (decrease of inhibition) of thalamic activity. The thalamocortical and corticostriatal projections are both excitatory (glutamate). The cortical neurons excite the population of GABAergic neurons within the caudate-putamen

that colocalizes SP. The GABA-SP+ striatal neurons then inhibit the neurons of GPi, reducing their activity and thus reducing their GABAergic inhibitory influence on VA/VL. This circuit is augmented by a second pathway that involves striatonigral projections, again involving the GABA-SP+ striatal neurons. They project to SNr neurons, reducing their activity and thus reducing their GABAergic inhibitory influence on VA. Due to the decrease in inhibition from both GPi and SNr, the dorsal thalamic neurons are more spontaneously active and drive the excitatory neurons in neocortex, promoting movement.

In addition to the direct loop, the dorsal striatopallidal complex also has the shorter loop that involves the intralaminar nuclei, comprising a circuit of the caudate-putamen to the internal segment of the globus pallidus, to these intralaminar nuclei, and directly back to the caudate-putamen. This circuit also has a “net value” of +1 $[(+1)(-1)(-1) = +1]$, thus making it a supplemental direct loop.

The indirect loop (Fig. 24-16) inhibits movement. Its primary circuit involves the same structures as the direct loop but with the addition of two more synapses, one of which is inhibitory (GPe) and one of which is excitatory (subthalamic nucleus), resulting in a net inhibitory affect on the thalamus $[(+1)(+1)(-1)(-1)(+1)(-1) = -1]$. With excitatory input from

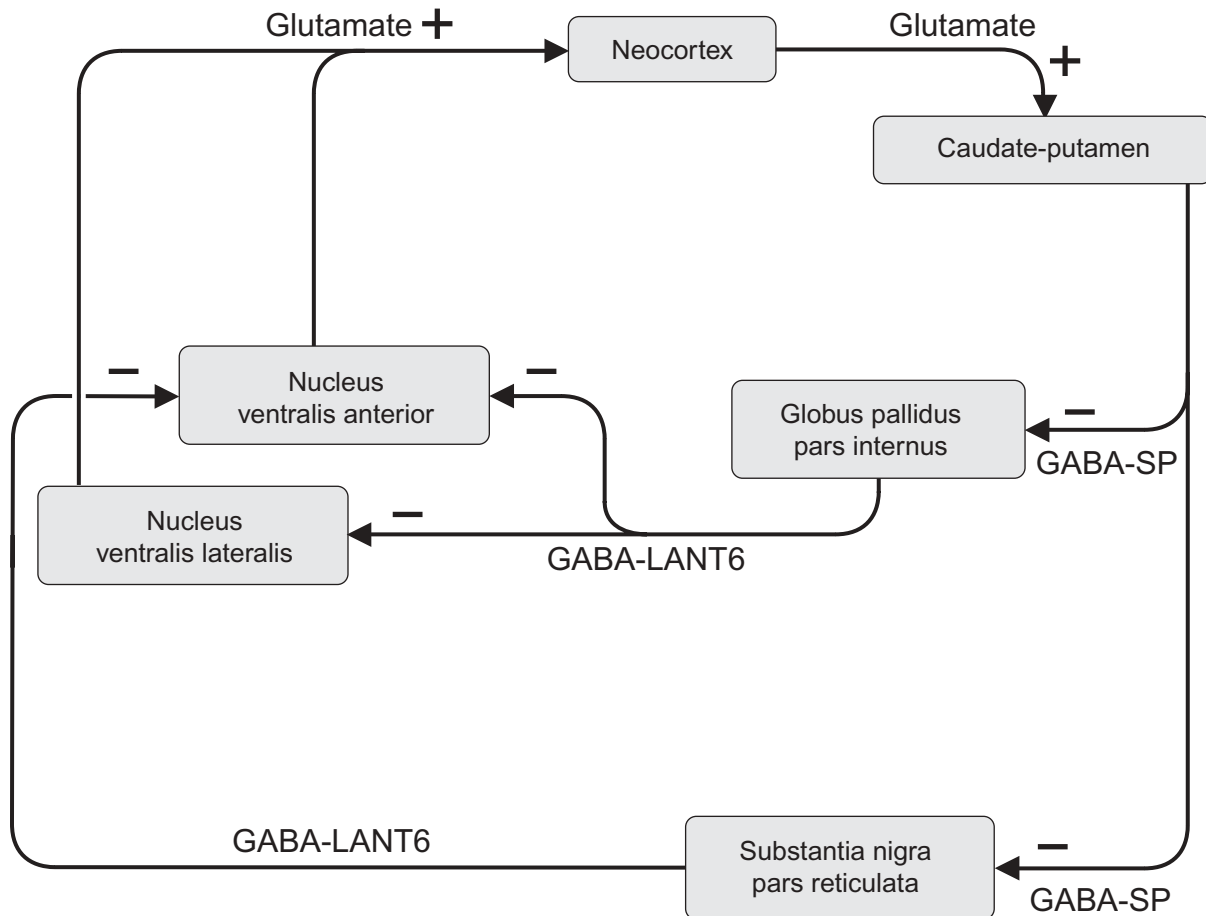


FIGURE 24-15. The direct loop of the dorsal striatopallidal complex in mammals.

neocortex, the population of GABAergic striatal neurons that colocalize ENK are stimulated. The GABA-ENK+ neurons project to GPe and inhibit its activity. The would-be inhibitory influence of GPe on the subthalamic nucleus is thus reduced, resulting in greater activity in the subthalamic nucleus. The latter is excitatory to GPi, which in turn is inhibitory to VA/VL. Thus, with cortical stimulation of the indirect loop, inhibition of the subthalamic nucleus is decreased, the activity in GPi increases, and activity in VA/VL therefore decreases, inhibiting movement. Like the direct loop, the indirect loop is also augmented by a second pathway that involves the substantia nigra, but this augmentation is via excitatory (glutamatergic) projections from the subthalamic nucleus to SNr, increasing the activity of the SNr neurons. Because the SNr input to VA is inhibitory, the thalamic activity is thereby decreased.

The many other inputs and connections of the structures (Figs. 24-12 to 24-14) involved in these loops affect their activity. Of key importance in this regard is the dopaminergic input from SNc to the caudate-putamen. This input stimulates the GABA-SP+ neurons and thus the activity of the direct loop, promoting movement. It also inhibits the GABA-ENK+ neurons, decreasing the activity of the indirect loop and thus decreasing its inhibitory influence on movement. In terms of our automobile analogy, this is akin to pressing down on the accelerator

and releasing the brake at the same time. Likewise, cerebellar influences can enter the system via cholinergic pedunculo-pontine projections to the subthalamic nucleus and the caudate-putamen and via direct projections of the deep cerebellar nuclei to VL. Additionally, neocortical activity drives the dorsal striatum and is itself influenced by a host of factors.

The ventral striatopallidal complex has connections that echo those of the dorsal complex. The ventral tegmental area and substantia nigra both have reciprocal connections with the ventral striatum, and the ventral pallidum is reciprocally connected with the subthalamic nucleus. The ventral striatum also receives an input from the intralaminar nuclei—particularly the more rostral and medial ones. The ventral pallidum projects to the intralaminar nuclei, the substantia nigra, the habenula, and the amygdala, which has reciprocal connections with the subthalamic nucleus as well as with both the ventral tegmental area and substantia nigra.

The second set of pathways of the ventral striatopallidal complex mimics the direct loop of the dorsal striatopallidal complex. This circuit is from prefrontal, olfactory, and limbic cortices through the ventral striatum to the ventral pallidum and from there to the mediodorsal nucleus of the dorsal thalamus, which in turn projects back to prefrontal cortex. Likewise, the ventral striatopallidal complex has the shorter,

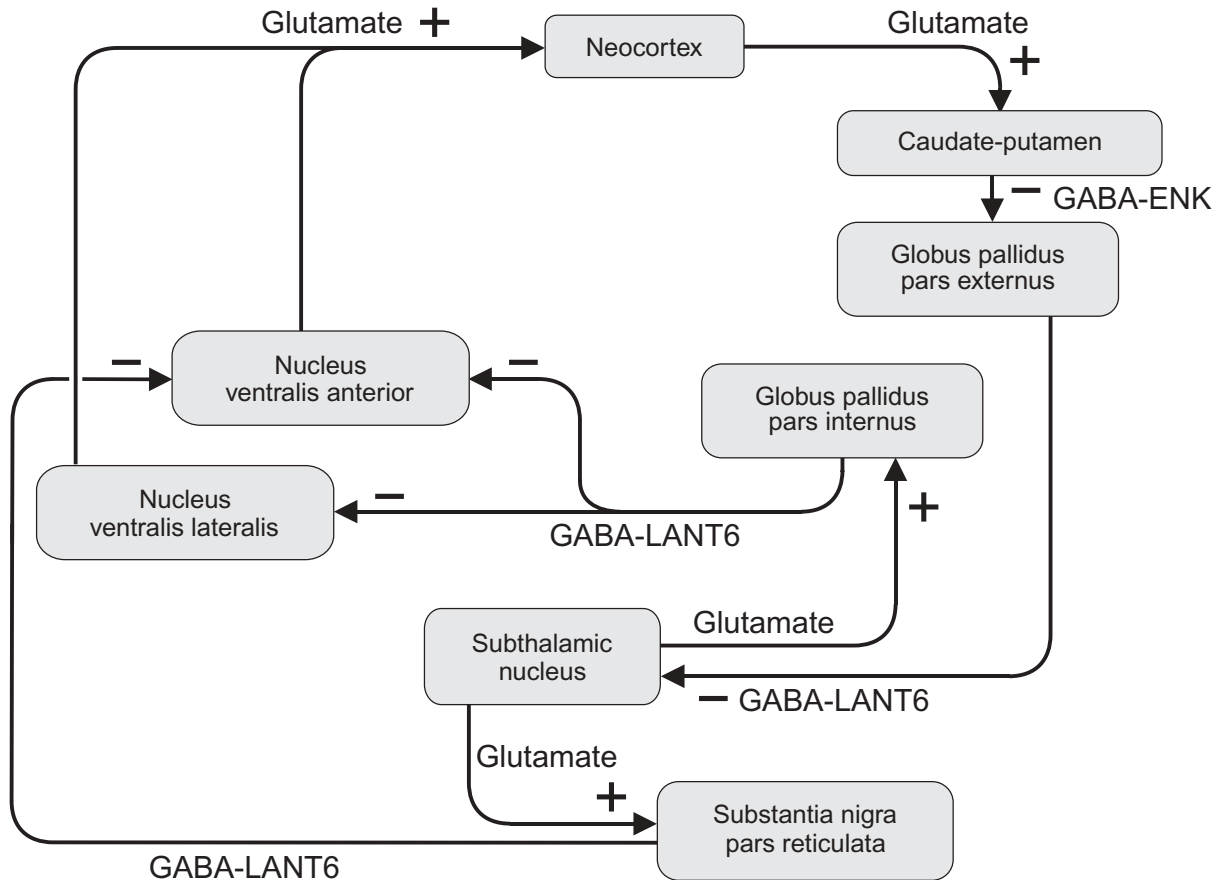


FIGURE 24-16. The indirect loop of the dorsal striatopallidal complex in mammals.

intralaminar loop from ventral striatum to ventral pallidum to the intralaminar nuclei and then directly back to the ventral striatum. Additionally, the ventral pallidum gives rise to a descending pathway to nucleus tegmenti pedunculopontinus pars compacta. The latter nucleus projects to the tectum via a relay in the substantia nigra and to the reticular formation.

The dorsal striatum and pallidum are thus more involved with neocortical structures, while the ventral striatum and pallidum are more involved with the limbic system. Nonetheless, inputs from both striatopallidal complexes interface in a number of different nuclei, including the habenula, amygdala, subthalamic nucleus, and tegmental nuclei, so that integration of information can occur. One of the most important of such integrative pathways is a projection from nucleus accumbens (primarily its core) to the dopaminergic neurons of the substantia nigra pars compacta, which in turn project directly to the caudate-putamen. Via this route, the ventral, more limbic parts of the striatum, which receive limbic cortical inputs, can affect the dorsal, more motor parts of the striatum.

The habenula receives projections from the ventral tegmental area (with its input from the ventral striatum) and directly from the dorsal pallidum. The amygdala receives projections from the ventral pallidum, has reciprocal connections with the ventral tegmental area and substantia nigra, and projects to both the dorsal striatum and the ventral striatum. The

subthalamic nucleus has reciprocal connections with the dorsal pallidum, substantia nigra, and amygdala, and it projects to the dorsal striatum. In the tegmentum, the substantia nigra, ventral tegmental area, and nucleus tegmenti pedunculopontinus pars compacta are all involved in multiple interconnections of the dorsal and ventral striatopallidal complexes.

Note that the projections discussed here are only some of those involved in this complex system. For example, neocortical projections to brainstem nuclei such as the ventral tegmental area have not been touched on, cortical projections of the dorsal striatum have been omitted, and a number of other connections and interconnections are also not included. We have chosen only some of the major pathways to illustrate the basic organization of the system here and have taken the risk of giving only a partial picture with the hope of not becoming lost in too much detail.

The Striatopallidal Complex in Nonmammalian Amniotes. The dorsal and ventral striatopallidal complexes of sauropsids (reptiles and birds) occupy the ventrolateral part of the telencephalon, ventral to the dorsal ventricular ridge. More detail is known about these complexes and their connections in birds than in reptiles. The circuitry and histochemical features in birds resemble those in mammals to an extensive degree, and the known features of this system in reptiles are consistent.

Thus, many of these features were likely present in the common amniote ancestor. The gain of the amniote circuitry, particularly involving pathways to the thalamus with subsequent relay to the pallium and back to the striatopallidum—the direct and indirect loops as described above for mammals—allowed for a greater repertoire of movements in those animals that invaded the complex and challenging land environment.

In reptiles (Fig. 24-17 and see Fig. 19-21), the dorsal striatum has characteristics shared across all amniotes, including a neuropil that stains heavily for AChE and CHAT due to its population of intrinsic cholinergic neurons, as well as GABAergic neurons that colocalize SP and ENK. Likewise, it receives a dopaminergic innervation by fibers that originate from mid-brain cell groups, including the substantia nigra pars compacta and the ventral tegmental area. The striatal components that separate into patch and matrix in mammals may also be present in sauropsids—both reptiles and birds—but they are not locally separated into distinct regions within the striatal territory. Concerning terminology, note that the medial part of the dorsal striatum in turtles was previously included in a region called area d, while the lateral part of the dorsal striatum was designated as the paleostriatum augmentatum (see Chapter 19).

The dorsal pallidum, i.e., the globus pallidus, of reptiles also shares features with that of mammals and birds. It contains the GABAergic perikarya of projection neurons that colocalize LANT6 and is densely innervated by striatopallidal GABA-SP+ and GABA-ENK+ woolly fibers. In contrast to the striatum, the dorsal pallidum is relatively poor in dopaminergic fibers and AChE. As in birds but in contrast to mammals, the pallidum in reptiles is a unitary structure, lacking anatomical differentiation into two distinct segments.

Some but not all of the basal ganglia circuits present in mammals and birds also have been identified in reptiles. Further work is needed to determine whether some of the indi-

vidual components have evolved separately in birds and mammals as a result of parallelism or are in fact general features of all amniotes. In reptiles, the dorsal striatum receives some input—apparently glutamatergic—from pallial regions. A thalamostriatal projection from nuclei homologous to the intralaminar nuclei of mammals has not been identified with certainty in reptiles, but the neuronal components of such nuclei may lie within the dorsomedial/dorsolateral part of the thalamus, which gives rise to widespread telencephalic projections. The dorsal striatum does have a reciprocal connection with the dopaminergic neurons of the midbrain tegmentum, as in all amniotes and most anamniotes as well, and it projects heavily to the dorsal pallidum. It also projects to the GABAergic neurons of the substantia nigra pars reticulata. The dorsal pallidum likewise projects to the latter as well as to a pretectal nucleus, called the **dorsal nucleus of the posterior commissure**, which in turn projects to the optic tectum.

A nucleus homologous to the mammalian VA/VL has not been identified in reptiles, although, like an intralaminar nuclear homologue, its components might reside within the dorsomedial/dorsolateral anterior, perirotundal part of the dorsal thalamus. This nucleus is an essential component of both the direct and indirect loops. As noted above, a nucleus homologous to the mammalian subthalamic nucleus, the anterior entopeduncular nucleus, is present in reptiles. In mammals, the subthalamic nucleus is a crucial component of the indirect loop. Whatever the circuitry of the dorsal thalamus in relation to the basal ganglia in reptiles, the major outflow of the dorsal striatopallidal system appears to be to the pretectum (see Chapter 20) and tegmentum, as is the case in amphibians.

A nucleus accumbens (see Fig. 19-21) and ventral pallidum are present in the rostral part of the telencephalon in reptiles. They correspond closely to their dorsal striatopallidal counterparts in the histochemistry of their neuronal components and innervation. In contrast to the dorsal striatum, nucleus accumbens receives its major dopaminergic fiber innervation from neurons of the ventral tegmental area rather than from the substantia nigra pars compacta. Among the other inputs to nucleus accumbens are those from the dorsal cortex and from the dorsomedial nucleus of the dorsal thalamus. The thalamic projection may be homologous to the intralaminar nuclear-striatal input present in mammals. Nucleus accumbens projects to the ventral pallidum, but the connections of the latter cell group remain to be specifically determined. Note that most of the cell group identified here as nucleus accumbens in turtles was previously called area c and also includes the ventral-most part of the formerly called area d (see Chapter 19).

In birds (Fig. 24-18), the dorsal striatum comprises the **lateral striatum** (previously called the paleostriatum augmentatum) and **medial striatum** (previously part of the territory called the lobus parolfactorius). Even though in mammals the dorsal striatum also comprises two separately named areas, the caudate nucleus and the putamen, it should be noted that the lateral striatum and medial striatum do not correspond to these two areas in a 1:1 manner. The avian dorsal striatal components exhibit high reactivity for AChE and CHAT, indicating the presence of intrinsic cholinergic neurons. They receive a substantial dopaminergic input from the substantia nigra pars compacta (A9), as well as from the ventral tegmental area (A10) and the retrorubral field (A8). The lateral striatum and medial

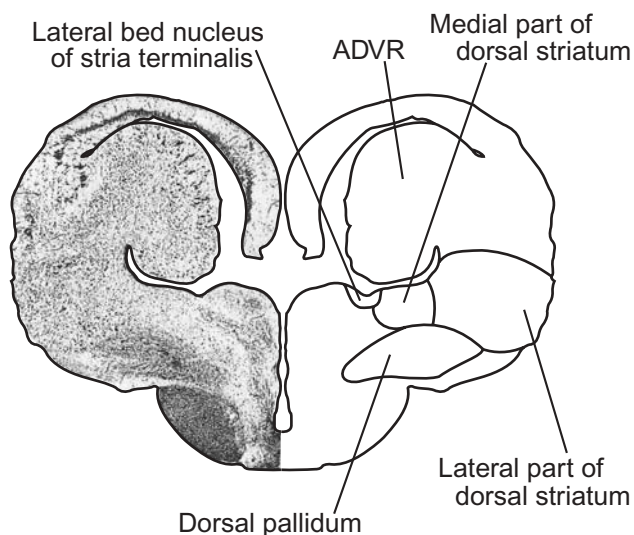


FIGURE 24-17. Transverse hemisection with mirror-image drawing through the telencephalon of a turtle (*Pseudemys scripta*). Adapted from Ulinski (1983) with modifications based on Powers and Reiner (1980) and Powers et al. (2003). Used with permission of John Wiley & Sons.

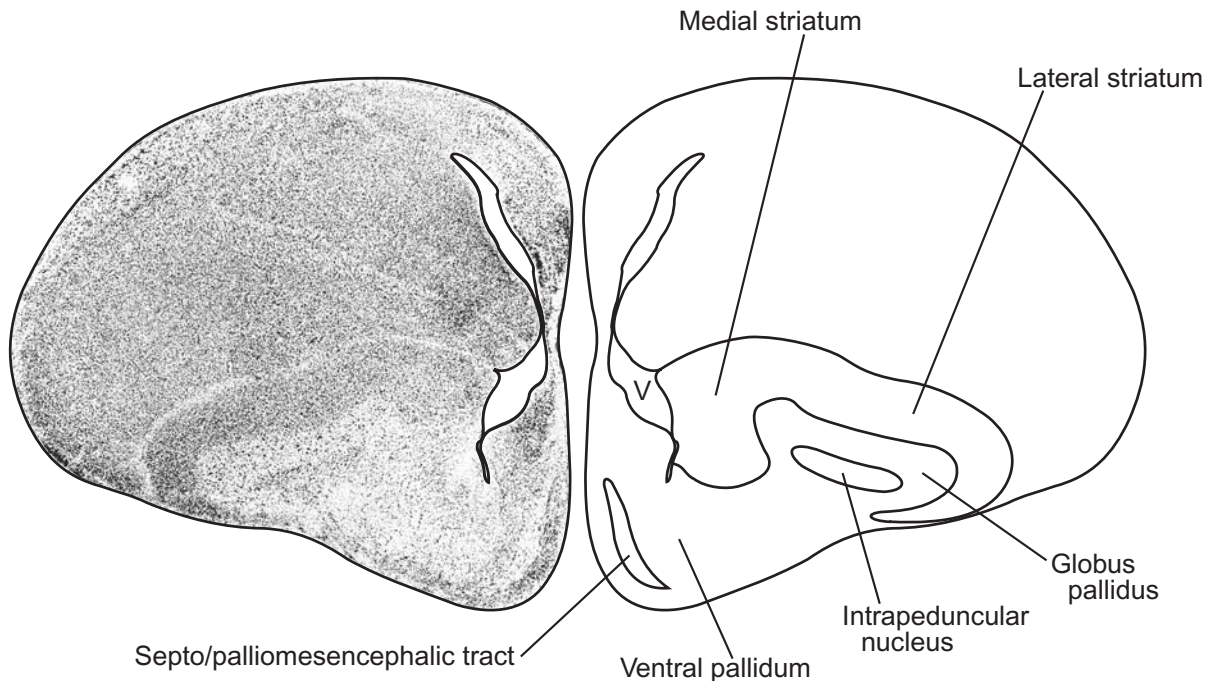


FIGURE 24-18. Transverse hemisection with mirror-image drawing through the telencephalon of the pigeon *Columba livia*. Adapted from Karten and Hodos (1967) and used with permission of The Johns Hopkins University Press.

striatum project to the **globus pallidus** and to both divisions of the substantia nigra in the midbrain tegmentum—its dopaminergic pars compacta and its GABAergic pars reticulata.

The dorsal striatal projection to the globus pallidus (previously called the paleostriatum primitivum) is substantial. In birds, only one division of the globus pallidus is apparent. However, it is innervated by both GABA-SP+ and GABA-ENK+ woolly fibers that arise from striatal neurons, and these projections terminate on different populations within the globus pallidus, so the anatomical basis for separate direct (Fig. 24-19) and indirect (Fig. 24-20) loops is present. In fact, the pallidal separation in mammals into two segments—the external receiving ENK+ GABAergic neuronal input and the internal receiving SP+ GABAergic neuronal input—may well be an example of parcellation (see Chapter 6), a mechanism proposed by Sven Ebbesson for the evolution of discrete, separate neuronal populations from more mixed, overlapping populations within a single region.

The projections of the globus pallidus include those to the pretectum for relay to the optic tectum. In birds, this pretectal nucleus is called **nucleus spiriformis lateralis** (see Chapter 20), the homologue of the dorsal nucleus of the posterior commissure of reptiles. As in other amniotes and in anamniotes, this pathway to the midbrain roof is involved in orienting behaviors and is a general feature of vertebrate brains.

Projections that appear to be amniote specializations are also present; the globus pallidus projects to avian diencephalic nuclei that correspond by their connections, histochemistry, and location to the mammalian intralaminar, VA/VL, and subthalamic nuclei. The intralaminar-like nuclei in birds are collectively referred to as the dorsomedial thalamic zone, or DTZ,

which includes three nuclei—**dorsomedialis (DM)**, **dorso-lateralis (DL)**, and **dorsointermedius posterior (DIP)**. The globus pallidus projects to DIP, just as it projects to the parafascicular nucleus within the intralaminar group of nuclei in mammals. The DTZ nuclei project to the dorsal striatum and also give rise to widespread pallial projections. They are situated in the same relative position within the dorsal thalamus as the mammalian intralaminar nuclei. Also corresponding to mammalian circuitry is a projection of the globus pallidus to a dorsal thalamic nucleus called the **ventrointermediate area (VIA)**, which corresponds to the ventral anterior (VA) and ventral lateral (VL) nuclei in mammals. This nucleus in birds receives input from both the substantia nigra pars reticulata and deep cerebellar nuclei, as does the VA/VL complex of mammals. It then projects to sensory- and motor-related pallial areas, particularly the rostral, somatosensory part of the Wulst, which in turn project back to the dorsal striatum. The globus pallidus likewise projects to the **subthalamic nucleus** (previously called the anterior nucleus of the ansa lenticularis). This nucleus comprises a population of glutamatergic neurons that project back to the globus pallidus.

The circuitry for both direct and indirect loops, as first defined in mammals, thus is present in birds as well. The direct loop (Fig. 24-19) consists of projections from the GABA-SP+ neurons of the dorsal striatum to GABAergic neurons of the globus pallidus. The latter population projects to the ventrointermediate area (VIA) of the dorsal thalamus, which in turn projects to the pallium. The pallium (rostral Wulst) then projects to the dorsal striatum, closing the loop. The GABA-SP input from striatum to the pallidum inhibits the GABAergic pallidal neurons, thus reducing their level of inhibitory influence on

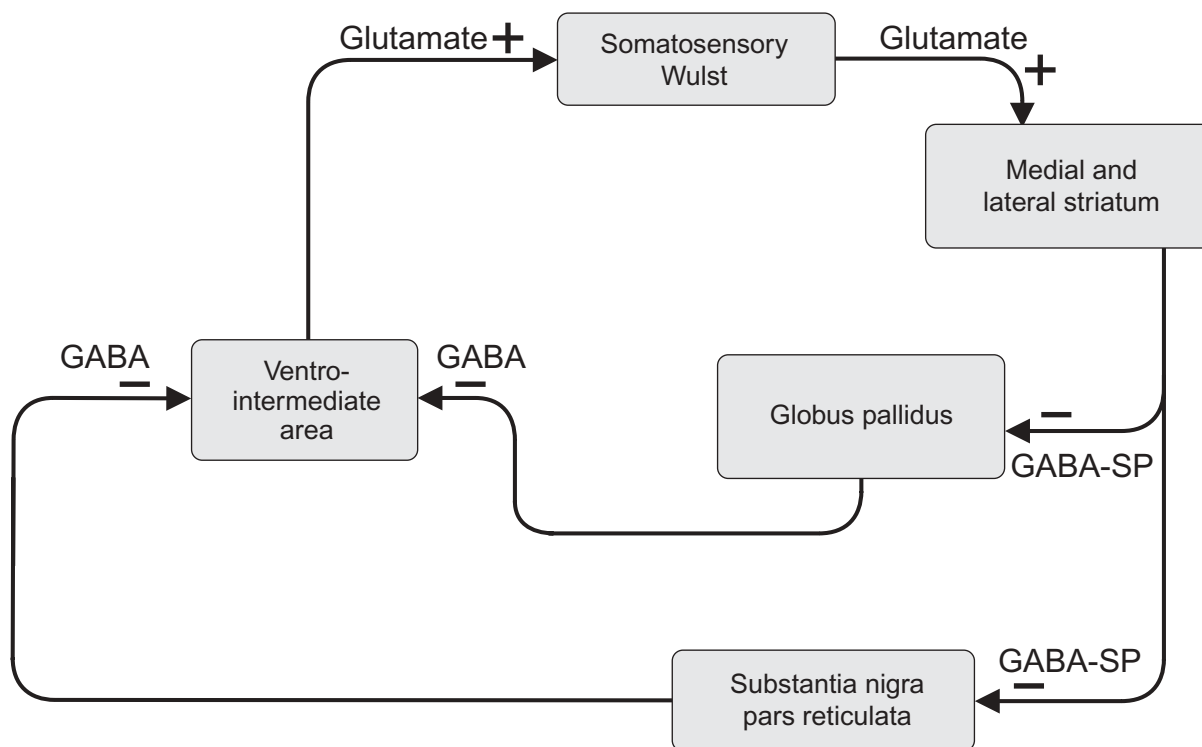


FIGURE 24-19. The direct loop of the dorsal striatopallidal complex in birds.

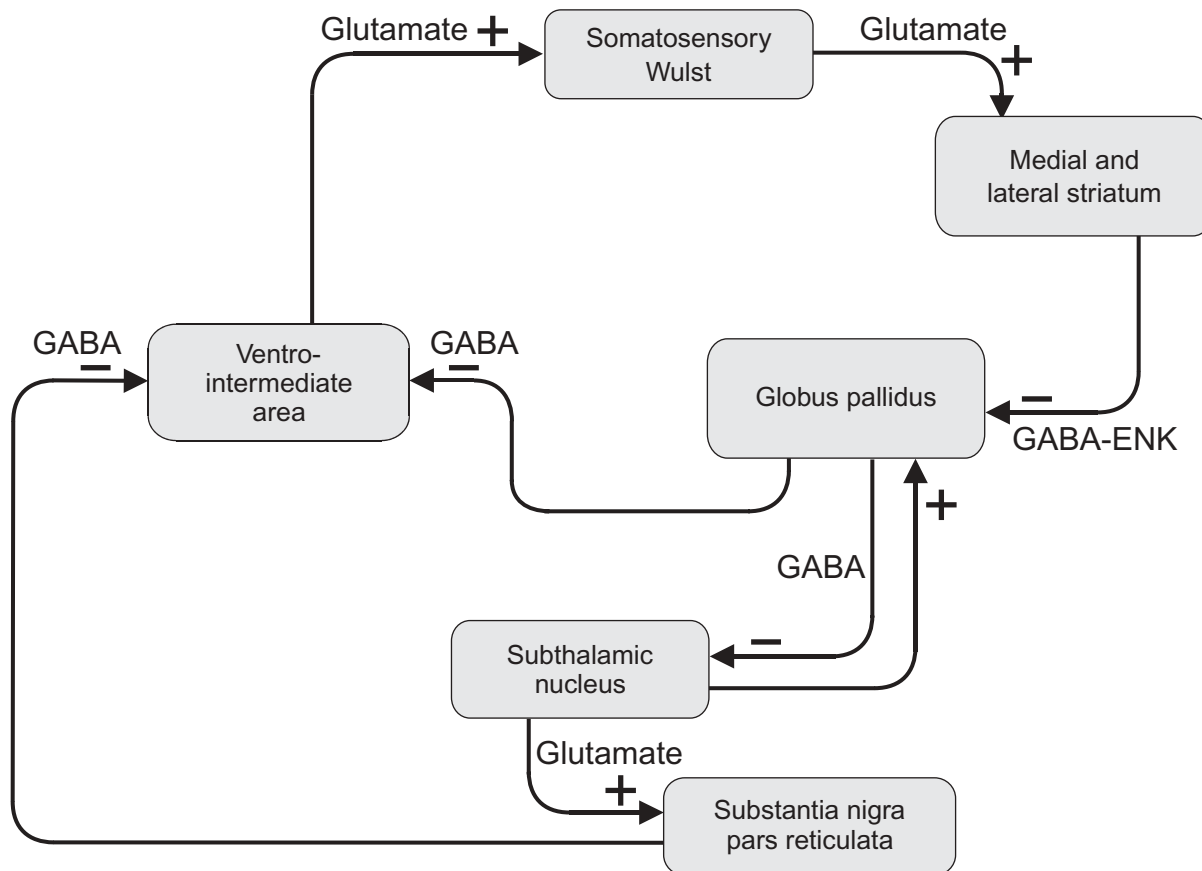


FIGURE 24-20. The indirect loop of the dorsal striatopallidal complex in birds.

VIA. A second component to the loop is formed by inhibitory GABA-SP+ striatal projections to the pars reticulata of the substantia nigra. The level of inhibitory influence that the latter can exert on VIA is likewise reduced. The spontaneous activity of the glutamatergic VIA neurons thus increases and promotes more pallial activity and an increase in glutamatergic pallial stimulation of the GABA-SP+ striatal neurons. The dopaminergic input to the striatum (not included in Fig. 24-19) likewise increases GABA-SP+ neuronal activity. The direct loop is a positive feedback loop $[(+1)(+1)(-1)(-1) = +1]$ that promotes the initiation of movement. Also as in mammals, the shorter, striatopallido-intralaminar loop for the dorsal striatopallidal complex is present as well and involves part of the DTZ.

The indirect loop (Fig. 24-20) also closely resembles that found in mammals. The GABA-ENK+ dorsal striatal neurons project to their target population of inhibitory neurons within the globus pallidus, which in turn project to the subthalamic nucleus. The subthalamic neurons are glutamatergic and project back to the globus pallidus. As with the direct loop, the globus pallidus projects to VIA, which projects to the rostral, somatosensory part of the Wulst, with the latter closing the loop by projecting to the striatum. The GABA-ENK+ input from the striatum to the pallidum inhibits the population of GABAergic pallidal neurons on which they terminate, thus reducing their level of inhibitory influence on the subthalamic nucleus. The spontaneous activity of the glutamatergic subthalamic neurons thus increases, resulting in increased stimulation of the other population of pallidal neurons that project to VIA. The inhibitory influence of the globus pallidus on VIA is thus increased, resulting in less activity of VIA neurons and less thalamic stimulation of the pallium. A second component to the loop is formed by excitatory subthalamic neuronal projections to the substantia nigra pars reticulata, which, like the globus pallidus, then increases its inhibitory influence on VIA. The indirect loop is a negative feedback loop $[(+1)(+1)(-1)(-1)(+1)(-1) = -1]$ that inhibits the initiation of movement. The dopaminergic input to the striatum (not included in Figs. 24-19 or 24-20) promotes movement, not only by stimulating GABA-SP+ neuronal activity of the direct loop but also by inhibiting the activity of the striatal GABA-ENK+ neurons and thus inhibiting the activity of the indirect loop.

An additional nucleus lies in the region of the dorsal striatopallidal complex—the **intrapeduncular nucleus** (Fig. 24-18). This nucleus is associated with the fibers of the lateral forebrain bundle as they come together ventromedial to the globus pallidus. It may be unique to birds. The histochemistry of its components and its embryological development suggest a striatal nature, but more information is needed about its connections and other characteristics before it can be definitively assigned to either striatal or pallidal territory.

The ventral striatopallidal complex in birds is quite well characterized in terms of its connections and histochemistry. Like the dorsal striatopallidal complex, it closely corresponds to its counterpart in mammals. A **nucleus accumbens** is present in the rostral part of the telencephalon; this cell group had previously been included as the ventromedial, rostral part of a region called the lobus parolfactorius, but it has now been renamed as nucleus accumbens. (It is now recognized that a nucleus previously called nucleus accumbens is in fact part of the bed nucleus of the stria terminalis). The second component

of the ventral striatum, the **tuberculum olfactorium**, also is present in birds. As in other amniotes, these ventral striatal components receive the better part of their dopaminergic innervation from the ventral tegmental area rather than from the substantia nigra pars compacta. Also, rather than mostly from sensory-motor areas of the pallium, their major pallial inputs arise from limbic-related regions. The ventral pallidum of birds consists of a previously unidentified group of GABAergic neurons that lie scattered among the fibers of the medial forebrain bundle, or fasciculus prosencephali medialis. These cells receive their major input from the ventral striatum. Their efferent projections are similar to those of the mammalian ventral pallidum, including some to the brainstem reticular formation and various cranial nerve nuclei. There is also a ventral pallidal projection to part of the DTZ, the dorsomedial thalamic zone, which appears to be comparable to the mammalian intralaminar nuclei. The DTZ in turn projects back to the ventral striatum.

THE STRIATAL AMYGDALA

In mammals, two nuclei of the amygdala are striatal—the **central amygdaloid nucleus** and the **medial amygdaloid nucleus**. The central amygdaloid nucleus comprises the **autonomic amygdala**, one of the four major divisions of the amygdala identified by Larry Swanson and Gorica Petrovich. It lies immediately ventral to the caudate-putamen and is in fact a ventral continuation of it (see Fig. 19-20). It receives its predominant inputs from parts of cerebral cortex, including prefrontal cortex, and from other divisions of the amygdala—the frontotemporal division of the amygdala (the lateral and anterior basolateral nuclei) and the main and accessory olfactory divisions. It also receives a dopaminergic input from the midbrain. Its hodological afferent pattern thus resembles that of the dorsal and ventral striatum. The efferent projections of the central amygdaloid nucleus also follow the striatal pattern. Within the subpallium, the central amygdaloid nucleus projects to the substantia innominata, and thus perhaps to ventral pallidal cells, and to the bed nucleus of the stria terminalis. Within the thalamus, it projects to several nuclei, including the centromedian and mediodorsal nuclei. It thus can participate in the striatopallidal loop systems. Additionally, the central amygdaloid nucleus projects to several sites predominantly related to the autonomic nervous system, including numerous hypothalamic nuclei, periaqueductal gray, dorsal motor nucleus of the vagus, and nucleus of the solitary tract. As for the rest of the striatum, it also projects to both the dopaminergic and GABAergic components of the substantia nigra.

The medial amygdaloid nucleus of mammals is a component of the accessory olfactory amygdala (see Chapters 19 and 29). It is a ventral continuation of the striatal territory, lying ventromedial to the central amygdaloid nucleus (see Fig. 19-20). It is reciprocally connected with the pallial components of this amygdalar division and, with them, receives a major input from the accessory olfactory bulb. Unlike the central amygdaloid nucleus, the medial amygdaloid nucleus receives projections from cortical areas, particularly part of frontal neocortex and the subiculum. Additional inputs arise in thalamic and hypothalamic nuclei. The predominant efferent target of

the medial amygdaloid nucleus is the medial part of the hypothalamus. In keeping with its striatal nature, it also projects to a number of other sites, including the bed nucleus of the stria terminalis and the reunions and mediodorsal thalamic nuclei. It also projects directly back to cortical areas.

In studies of hamsters, the vomeronasal-recipient medial amygdaloid nucleus has been found to play a crucial role in male copulatory behavior. Lesions restricted to this nucleus markedly diminish the male's licking and sniffing of the female's anogenital region and eliminate the male's mating behavior. The medial amygdaloid nucleus is thus believed to be crucial for the relay of chemosensory information to preoptic and hypothalamic regions involved in the mediation of sexual behaviors.

The central and medial amygdaloid nuclei show cytoarchitectonic continuity with the lateral and medial bed nuclei of the stria terminalis and also with cell columns in part of the substantia innominata. These structures all give rise to projections to the hypothalamus, and, as discussed in Chapter 19, they have been characterized as the extended amygdala.

In birds, two subpallial components of the amygdala have been identified. Most or all of the medial part of a nucleus called **nucleus taeniae of the amygdala** is subpallial. This region may correspond to the medial amygdaloid nucleus of mammals, even though birds lack a vomeronasal, accessory olfactory system. A second region called the **subpallial amygdala** lies ventral to the globus pallidus. This region resembles part of the extended amygdala of mammals in connections, neurochemistry, and location. Whether a structure that corresponds specifically to the mammalian central amygdaloid nucleus is present in birds has not yet been determined.

Among reptiles, subpallial amygdalar territory has been identified within the basal telencephalon of turtles. Based on dopaminergic and acetylcholinesterase histochemistry, the putative central amygdala of turtles lies ventromedial to the striatum proper, as is the case in mammals. Immediately medial to it lies the lateral part of the bed nucleus of the stria terminalis. A medial amygdaloid nucleus also appears to be present in the ventral-most part of the caudal pallium, even though turtles, like birds, lack a vomeronasal organ and accessory olfactory system. This nucleus receives olfactory input from the main olfactory bulb and may contribute to the stria terminalis, projecting to the hypothalamus. Its position corresponds to that of the nucleus taeniae of the amygdala of birds. It also resembles the mammalian medial amygdaloid nucleus in its histochemical properties.

In lizards, a region called the striato-amygdaloid transition area, which lies in the caudal part of the dorsal ventricular ridge, has connections similar to those of the central amygdaloid nucleus of mammals and is a good candidate for its homologue. Lesions of the striato-amygdaloid transition area result in a decrease of tonic immobility in response to threat, suggesting that its functional role is similar to that of the central amygdaloid nucleus in mammals, i.e., it is involved in fear responses to perceived threats.

Within amphibians, subpallial amygdalar components have been found in anurans. Within the amygdalar components of the telencephalon (Fig. 24-5), both pallial and striatal amygdalar regions are present. The pallial parts include the anterior amygdalar area, the lateral amygdala, and the more rostral part

of the medial amygdala. The striatal region of the amygdala comprises the **central amygdala** and the more caudal, periventricular part of the **medial amygdala**. Both of these striatal nuclei receive a substantial dopaminergic input from the midbrain. The medial amygdala receives a substantial input from the vomeronasal system and has reciprocal connections with the hypothalamus. A **bed nucleus of the stria terminalis** lies medial to the caudal part of the medial amygdala. The striatal amygdalar components and the bed nucleus of the stria terminalis constitute a homologue of the extended amygdala of mammals. As discussed in Chapter 29, various nuclei within the subpallium of ray-finned fishes may be amygdalar in nature, but additional work needs to be done to resolve current questions.

CHOLINERGIC NEURONAL POPULATIONS OF THE BASAL TELENCEPHALON

Nucleus basalis (of Meynert), sometimes called the **magnocellular corticopetal cell complex**, is one of four major groupings of cholinergic neurons in the basal forebrain of mammals, named **Ch1–Ch4** by Marek-Marsel Mesulam and his co-workers. In addition to nucleus basalis, which is the Ch4 group, cholinergic neurons are distributed within the **medial septal nucleus** (Ch1) and in the **vertical** (Ch2) and **horizontal** (Ch3) **limbs of the nucleus of the diagonal band of Broca**. The latter is an L-shaped nucleus that lies within the medial part of the basal forebrain, ventral to the septal region. In fact, the cholinergic neurons within the medial septal nucleus (see Chapter 30) are in continuity with those in the nucleus of the diagonal band.

The Ch4 group, nucleus basalis, projects widely to cortical areas and to the amygdala. The medial septal cholinergic neurons, Ch1, project to the hippocampus. The Ch2 neurons of the diagonal band project to the hippocampus and the hypothalamus, while its Ch3 neurons project to the olfactory bulb. In mammals, cholinergic neurons within nucleus basalis project to all areas of neocortex. In turtles, similarly located cholinergic neurons (see Fig. 19-28) that lie within the ventral paleostriatum and globus pallidus have been found to project to the dorsal cortex. In birds, the corresponding population of cholinergic neurons has been renamed as nucleus basalis magnocellularis. (The previously named avian nucleus basalis, which receives multiple sensory inputs and is altogether a different structure, has been renamed nucleus basorostralis pallii.) As in other amniotes, the cholinergic nucleus basalis magnocellularis of birds globally innervates the pallium.

The septal nuclei will be discussed in Chapter 30. However, we should note here that there are significant differences among amniotes in terms of the distribution of cholinergic neurons within this region. Cholinergic neurons are notably absent from the septal region in lizards, whereas, in birds, they are present but they are located within the lateral rather than the medial part of the septum. As in mammals, these neurons project to the hippocampus. Although less data are available on cholinergic neurons in the basal telencephalon of anamniotes, such neurons may be widely distributed among vertebrates. Whether they tend to occur in several discrete

regions that correspond to those in amniotes has not yet been determined. Cholinergic neurons are present in the striatal and septal regions in frogs. Among ray-finned fishes, cholinergic neurons have been identified in the lateral part of the area ventralis (VI) in the telencephalon of a cyprinid teleost and a trout. In the trout, these neurons project into the dorsal, pallial part of the telencephalon and may thus have a role similar to that of the nucleus basalis cholinergic cells of amniotes.

EVOLUTIONARY PERSPECTIVE

A dorsal striatopallidal complex in the ventrolateral part of the telencephalon has been identified in most major radiations of vertebrates. Whether a homologous dorsal striatopallidal complex is present in hagfishes and ray-finned fishes remains to be definitively resolved, but it appears to be a shared feature of lampreys, cartilaginous fishes, and tetrapods. The anamniote-amniote transition was marked by major changes in striatopallidal components and connections. The dorsal striatum of anamniotes is relatively poor in intrinsic neurons, particularly cholinergic neurons, and at the transition, it gained substantially in this regard. In amniotes, the striatum is exceptional for its dense AChE and CHAT staining. In amniotes, some circuits shared with anamniotes are retained, including reciprocal connections between posterior tuberculum and/or midbrain dopaminergic neuronal populations and the dorsal striatum as well as striatopallidal projections to the midbrain tectum via direct and/or indirect pathways. The midbrain tectal pathways may be important for orienting movements to salient stimuli.

Other circuits—particularly the direct and indirect loops that involve a striatopallidal pathway to the dorsal thalamus and thence to the pallium—appear to be absent in anamniotes and, within amniotes, may have evolved separately, at least to some extent, in birds and mammals. These pathways are concerned with regulating the initiation of voluntary movements and the suppression of involuntary ones and are correlated with the demands and challenges of the highly complex land environment. With the gain of these loops, the newly expanded pallium of amniotes also took over as the dominant source of input to the striatum, allowing its analyses and correlations of sensory stimuli to strongly affect striatopallidal activities. Also correlated in this regard was the gain or marked increase of generalized, alerting excitation of the striatum by inputs from intralaminar nuclei in mammals and their homologues in birds and perhaps reptiles as well. The dopaminergic inputs to the striatum were retained from the ancestral condition, as were their differential functional affects—excitatory to striatal SP+ neurons and inhibitory to striatal ENK+ neurons—but a major shift occurred with the predominance of striatopallidal outflow now being directed through the dorsal thalamus and from there back to the pallium.

The evolution of the ventral striatopallidal complex is less well understood, at least among anamniotes. The ventral striatum and pallidum are clearly present in both urodele and anuran amphibians and thus appear to have been features of the ancestral tetrapod stock, but their presence or absence in ray-finned and cartilaginous fishes and in jawless vertebrates remains an open question. They are more closely associated in

terms of connections with the ventral tegmental area rather than with the substantia nigra pars compacta, and since cartilaginous fishes have both of these tegmental dopaminergic cell groups, this group of vertebrates may well have a ventral striatopallidal system as well, comprising at least the tentatively identified nucleus accumbens.

Both pallial and striatal components of the amygdala have been identified across tetrapods. The striatal components include medial and central nuclei, as well as a bed nucleus or nuclei of the stria terminalis. These components are thus plesiomorphic for at least tetrapods. The dorsomedial part of the pallium in ray-finned fishes may be a homologue of part or all of the mammalian pallial amygdala; various nuclei within the subpallium, area ventralis, may constitute a striatal component of the amygdala, but this possibility remains to be verified. Information on amygdalar structures is meager for cartilaginous fishes and agnathans.

Cholinergic neurons are present in four regions of the basal telencephalon in mammals—the medial septum, the vertical and horizontal limbs of the nucleus of the diagonal band of Broca, and nucleus basalis. While subpallial cholinergic cell populations are a general feature of vertebrates, the exact correspondences between taxa have not yet been delineated. The nucleus basalis, Ch4 population appears to be plesiomorphic for at least amniotes. Nucleus basalis, also known as the magnocellular corticopetal cell complex, has wide projections to neocortex in mammals and projects to cortical regions in the nonmammalian amniotes that have been studied. Cholinergic cells that may correspond to nucleus basalis also have been found in some anamniotes, including amphibians and some ray-finned fishes. However, the presence of a cholinergic cell population in the ventral part of the telencephalon is not completely consistent across vertebrate taxa. Such a population is apparently absent in one species of lamprey but present sparsely in another, while it is absent in the cartilaginous fishes studied to date and in a sturgeon. Such a cell population either has evolved several times independently or is a generalized ancestral feature that has been lost in several lines.

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25

Nonlimbic Pallium

INTRODUCTION

In all groups of jawed vertebrates, the telencephalic pallium can be divided into at least three areas—the **medial, dorsal, and lateral pallia**—and recent evidence indicates a fourth area that lies ventral to the lateral pallium, which is called the **ventral pallium**. The medial pallium and the olfactory-recipient parts of the lateral pallium can be classified as limbic pallium, in the broader sense of the term limbic. The remaining part of the pallium, the nonlimbic pallium, is addressed in this chapter. In vertebrates with fully everted telencephalons, i.e., ray-finned fishes, comparable pallial areas are present in transposed topographical order. In amniotes, the Group IIB vertebrates, the nonlimbic pallium forms a large part of the telencephalon and receives ascending sensory projections from the dorsal thalamus.

While a dorsal part of the pallium lying between the medial and lateral pallia has been identified in all jawed vertebrate groups, the question of whether any or all of the dorsal pallium in various anamniotes is homologous to the nonlimbic pallial areas in amniotes is one of the most important unresolved questions in comparative neurobiology. Put simply, did a nonlimbic pallium homologous to that in extant amniotes exist in the earliest vertebrates, or has a nonlimbic pallial, ascending sensory-receptive part of the telencephalon been evolved separately in several vertebrate lineages? If it has evolved separately in historical, phylogenetic terms, to what extent is it specified by the same patterning genes and thus syngenous, as some recent evidence indicates? In attempting to fully resolve these questions, comparative neuroanatomists have focused on several defining features of the nonlimbic

pallium in amniotes, including the receipt of ascending sensory projections from the diencephalon and the absence of afferent projections from the olfactory bulb.

This chapter begins with an overview of areas identified as dorsal pallium in anamniotes. The medial (limbic) pallium of anamniotes with evaginated pallia is also mentioned in terms of its receipt of major ascending sensory pathways, a condition not present in amniotes. The nonlimbic pallium in amniotes is then addressed. Recent embryological findings in amniotes and also in some anamniotes suggest that three of the four recently identified pallial components—dorsal, lateral, and ventral—contribute embryologically to the pallial region we are considering here. The major components of the nonlimbic pallium in mammals are discussed, including a brief overview of the higher-level, association neocortical areas. The nonlimbic pallial areas in sauropsids are then noted, and a summary of the ascending pathways from dorsal thalamic nuclei (see Chapter 22) is given. As discussed in Chapter 19, the frontotemporal division of the amygdala is in receipt of collothamic projections and is much more closely associated with neocortical sensory areas than with “limbic” pallial components. This division of the amygdala is therefore included in this chapter. Given the continuing debate over the relationship of collopallial areas among amniotes, we felt it important to conclude this chapter with a summary of some of the work that has been done on the cognitive abilities of birds. The dorsal ventricular ridge and Wulst pallial regions in birds support some highly complex cognitive capabilities. The similarities of circuitry with pallial areas in mammals, despite marked dissimilarities of cytoarchitecture, may be one of the key features that allow for these functions.

THE NONLIMBIC PALLIUM IN GROUP I VERTEBRATES

In lampreys [Fig. 25-1(A)], a small region that receives olfactory input has been tentatively identified as the dorsal pallium, but its identity as such is questionable, since it may instead lie within the subpallium. It is thus not labeled in Figure 25-1. In squalomorph sharks, electrophysiological evidence indicates that both the medial and dorsal pallia [Fig. 25-1(B)] receive visual input, but anatomical tracing studies of thalamic projections need to be done.

In nonteleost ray-finned fishes, as noted in Chapter 3, the areal topography is thought to be reversed in everted pallia (C-B-A) versus evaginated pallia (A-B-C), but with the topology, the

ordinal sequence, preserved. In Type I brains, such as that of the bichir *Polypterus*, the **dorsolateral pallium** [Fig. 25-1(C)] comprises the more distal part of the pallium. It previously was designated as two areas, P2 and P3, which were thought to correspond topologically to the dorsal and medial pallia of vertebrates with evaginated telencephalons, respectively. Both of these pallial areas, now called the medial and lateral subdivisions of the dorsolateral pallium, receive a sparse olfactory input, and they also both receive more substantial inputs from the subpallium and from a nucleus within the posterior tuberculum called nucleus medianus. The latter nucleus relays visual inputs from the optic tectum to the dorsolateral pallium. Neither of the two pallial subdivisions receives any ascending inputs from the dorsal thalamus. Likewise in sturgeons, which have a relatively simple telencephalic pallium in terms of

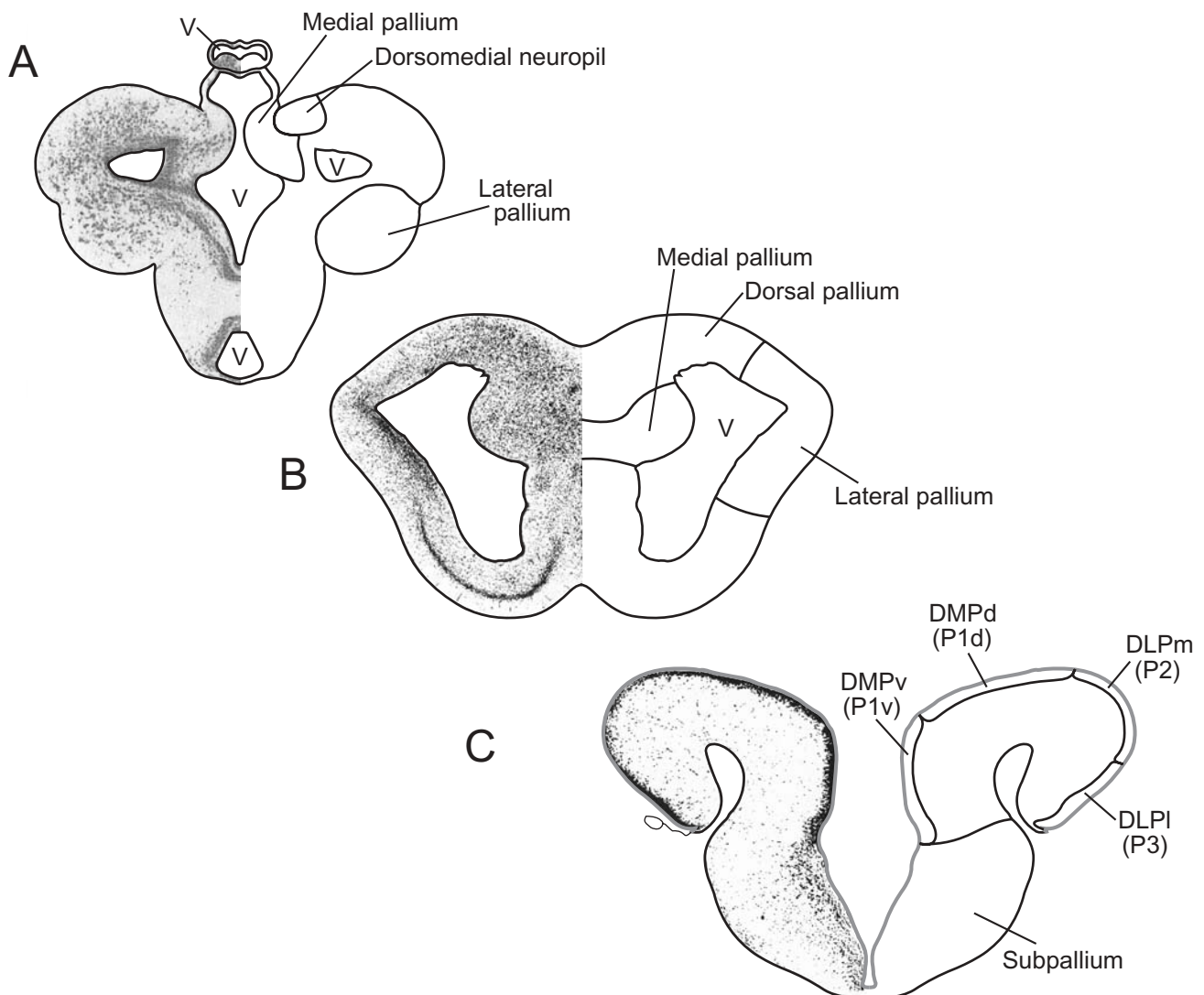


FIGURE 25-1. Transverse hemisections with mirror-image drawings through the telencephalons of a lamprey (*Ichthyomyzon unicuspis*) (A), a squalomorph shark (*Squalus acanthias*) (B), and a bichir (*Polypterus palmatus*) (C). A is adapted from Northcutt and Wicht (1997) and used with permission of S Karger AG, Basel. B is adapted from Northcutt et al. (1988) and used with permission of John Wiley & Sons. C is adapted from Northcutt and Davis (1983) and used with permission of the University of Michigan Press.

limited cell migration from the ventricular surface, ascending sensory projections from dorsal thalamic nuclei to the distal part of the pallium have not been found. Ascending thalamic projections may have been present in the stem ray-finned fishes ancestrally and subsequently lost to these relatively neotenic pallia, or they may have been independently evolved in the neopterygian ray-finned fishes (gars, *Amia*, and teleosts) in conjunction with the greater elaboration of pallial areas.

In lungfishes, the dorsal pallium [Fig. 25-2(A)] receives olfactory bulb input, but possible ascending thalamic projections to the medial and/or dorsal pallia have not yet been studied. In the crossopterygian fish *Latimeria*, the telencephalic pallium is partially everted [Fig. 25-2(B)], similar to the pallial eversion seen in ray-finned fishes. Thus, the ventricular space extends dorsally along the surface of the dorsome-

dial pallium. Several pallial regions have been identified on topographical grounds, but how the organization of the pallium in *Latimeria* corresponds to that of other vertebrate groups is unknown.

In frogs, the rostral part of the dorsal thalamus (nucleus anterior) relays a variety of nonvisual sensory inputs to both the medial and dorsal pallia [Fig. 25-2(C)]. The lateroventral part of the pallium comprises multiple regions, including the lateral cortex, lateral amygdala, and anterior amygdalar area. The olfactory bulb projects to the lateral cortex and lateral amygdala, and it additionally projects to the ventral part of the dorsal pallium. Recent molecular data support the division of the lateroventral pallium in frogs into two distinct pallial regions, a **lateral pallium** and a newly recognized fourth pallial region, the **ventral pallium**. The latter region lies

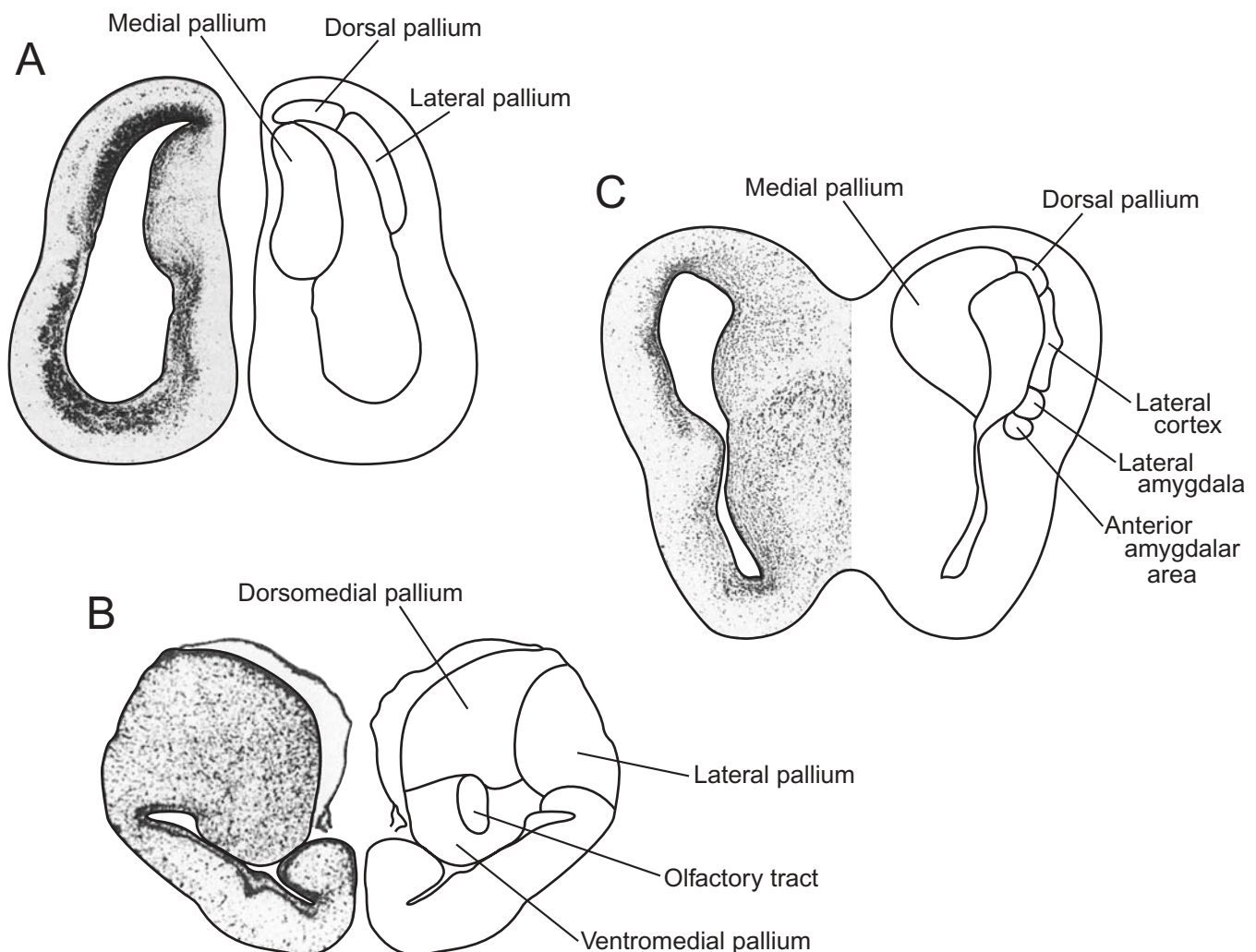


FIGURE 25-2. Transverse hemisections with mirror-image drawings through the telencephalons of (A) a lungfish (*Protopterus annectens*), (B) the crossopterygian fish *Latimeria*, and (C) a bullfrog (*Rana catesbeiana*). A is adapted from Reiner and Northcutt (1987) and used with permission of John Wiley & Sons. B is adapted from Northcutt (1995) and used with permission of S Karger AG, Basel. The identification of areas is based on Nieuwenhuys and Meek (1990). C is adapted from Wilczynski and Northcutt (1983) with the identification of areas based on Marin et al. (1998) and used with permission of John Wiley & Sons.

ventral to the lateral pallium and is also present in amniote brains. Both of the lateral and ventral pallial areas contribute to the lateral cortex [Fig. 25-2(B)] during embryological development, but only the ventral pallium gives rise to the lateral amygdala.

The possibility that the dorsal pallium and parts of the lateral and ventral pallia in frogs are homologous to the nonlimbic pallium of amniotes has been raised on the basis of similarities in histochemistry, cellular continuity, and embryological data. However, where to draw the dividing line between the dorsal and medial pallia is presently unclear, and differences in the pattern of dorsal pallial projections exist between frogs and salamanders.

THE NONLIMBIC PALLIUM IN GROUP IIA VERTEBRATES

Neuroanatomical Organization

In hagfishes, the entire pallium (Fig. 25-3) is in receipt of olfactory projections, and ascending projections from the

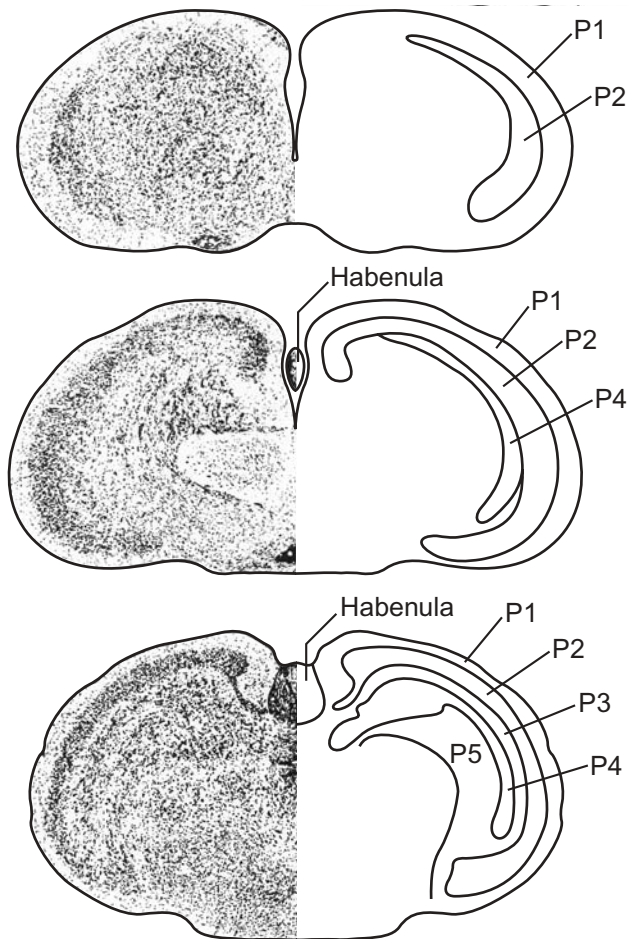


FIGURE 25-3. Transverse hemisections with mirror-image drawings through the telencephalon of a hagfish (*Eptatretus stouti*). The top section is most rostral. P1–P5 are pallial areas. Adapted from Wicht and Northcutt (1992) and used with permission of S Karger AG, Basel.

diencephalon have not been studied. In Group II cartilaginous fishes, some data are available on visual, auditory, and lateral line projections to the telencephalon. Auditory responses have been recorded in the telencephalon of sharks, with the best responses being in a medial area within the middle part of the hemisphere. Within the telencephalon of Group II (galeomorph) sharks [Fig. 25-4(A)], a large nucleus, called the **central nucleus**, is present in a central location. An area designated as dorsal pallium lies dorsal to the central nucleus, but the central nucleus is believed to also be a part of the dorsal pallium. The dorsal pallium is richly populated with a substantial variety of different neuronal cell types.

In galeomorph sharks, ascending visual projections from the rostral part of the dorsal thalamus (nucleus anterior) terminate within the central nucleus. Visual projections from the tecto-recipient dorsal posterior nucleus in the dorsal thalamus may likewise terminate in the central nucleus, as well as in the

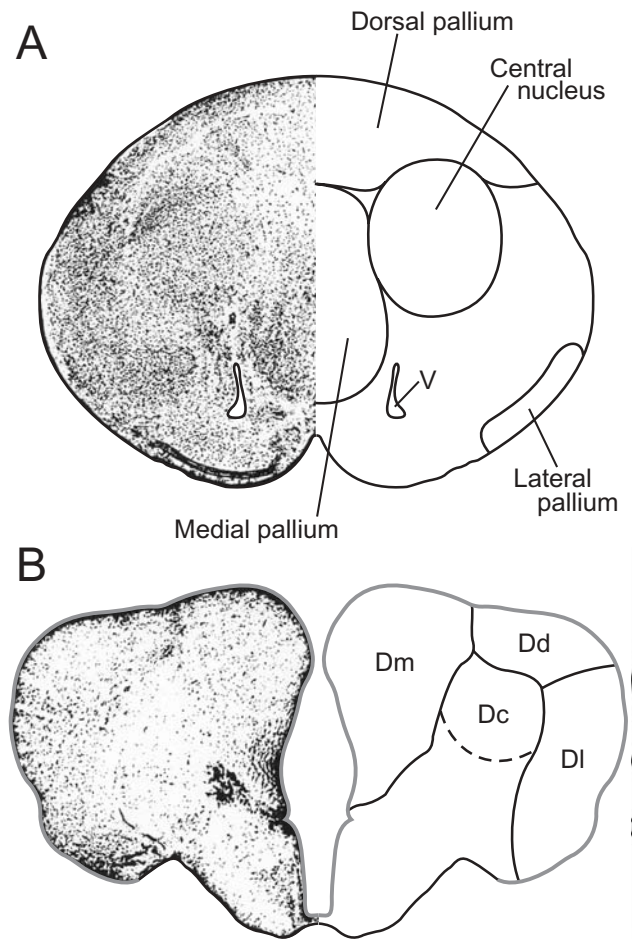


FIGURE 25-4. Transverse hemisections with mirror-image drawings through the telencephalons of (A) a galeomorph shark (*Ginglymostoma cirratum*) and (B) a teleost fish (*Lepomis cyanellus*). Dc, Dd, Dl, and Dm = central, dorsal, lateral, and medial zones of the area dorsalis telencephali, respectively. A is adapted from Ebbesson (1980) and used with kind permission of Springer Science and Business Media. B is adapted from Northcutt and Davis (1983) and used with permission of the University of Michigan Press.

striatum. Visual evoked potentials have also been recorded in both the dorsal and medial pallia. Visual potentials have similarly been recorded in the medial pallium of skates, to which nucleus anterior projects. Behavioral studies have shown that sharks can discriminate patterns after surgical removal of their optic tecta, indicating that their telencephalic visual areas mediate this function.

In skates, a telencephalic area has been identified electrophysiologically in which both electrosensory and visual responses can be recorded. This area is within the medial pallium, and nucleus anterior of the dorsal thalamus, the posterior tuberculum, and the electrosensory lateral posterior nucleus are known to project to it. The evolutionary relationship of the dorsal and medial pallia to each other in cartilaginous fishes and of both to the nonlimbic pallium of amniotes remains unclear.

The telencephalon in teleosts is a complex and only partly understood area of the brain. A dorsally lying pallial region, the **dorsal zone of area dorsalis telencephali (Dd)**, is shown in the brain of the green sunfish in Figure 25-4(B), as is the more laterally, or distally, lying region, the **lateral zone of area dorsalis telencephali (Dl)**, which has multiple parts. In the common goldfish, the dorsal part of this area, **Dld**, has been found to receive projections from the retino-recipient nucleus anterior in the dorsal thalamus and is implicated in visual functions by its metabolic activity and electrophysiology. Dld thus may be homologous to at least part of the dorsal pallium of other vertebrates. However, pallial projections from nucleus anterior have not been found in several other species of teleosts, and in goldfish, the visual input to Dld may be via a multisynaptic relay that includes the optic tectum.

A large motor region also is present within the putative dorsal pallial area of the telencephalon in goldfish, which includes the dorsal zone of area dorsalis, Dd. Two motor representations of the head and body have been identified by Cosme Salas, Fernando Rodríguez, Cristina Broglio, and their co-workers and called **fishunculi**, the piscine version of the motor and somatosensory representations in humans, which are called homunculi. Rostral to the fishunculi are two regions that control movements of the eyes, similar to the motor eye fields in mammalian brains. The motor representations lie medial to the visual and the more distally situated hippocampal (see Box 30-1) pallial regions and thus appear to form the medial half of the dorsal pallial region. The motor and visual regions in the goldfish pallium may correspond to the nonlimbic lemnopallium of amniotes. Whether this correspondence is a case of phylogenetic homology, only of generative homology, or of convergence is not yet known.

Transverse hemisections through the telencephalon of a variety of ray-finned fishes are shown in Figure 25-5. This figure includes a more detailed treatment of the pallial areas in the sunfish than that in Figure 25-4. The pallium of ray-finned fishes exhibits a wide range of variability in its degree of elaboration. It has a relatively simple and laminar structure in basal ray-finned fishes, bichirs and sturgeons, and a more extensive degree of neuronal cell production and migration in neopterygians, which include gars and the rest of the taxa shown in this figure. Note that, even within euteleosts (e.g., the sunfish, catfish, and squirrelfish), the degree of elaboration varies

markedly. In squirrelfish, the periventricular zone, labeled Dms, Dld, and Dlv in the figure, forms a highly elaborate, cortex-like set of strata, particularly in its lateroventral sector. The degree of eversion also varies considerably across these taxa, but it is important to note that the degree of eversion is not correlated with the degree of areal elaboration. Rather, the two factors vary independently. For example, in both bichirs and euteleosts, the degree of eversion is quite extensive, with the ependymal attachment coming off the hemisphere at about seven o'clock on the left side. In gars, which are intermediate phylogenetically, the opposite end of the scale is evinced: the ependymal attachment comes off the hemisphere at only about eleven o'clock on the left side.

Two additional pallial regions that flank the region of Dd and Dld appear to be limbic in nature rather than nonlimbic. We have included a brief overview of them here for perspective, since some major questions about pallial organization in ray-finned fishes remain to be answered.

The more ventral part of Dl, Dlv, appears to be a homologue of the hippocampus (medial pallium) of other vertebrates (see Chapter 30). It lies in the topologically corresponding position. The telencephalic hemisphere shown in the catfish in Figure 25-5 is rather similar to that of the goldfish, including the dorsomedial and dorsolateral parts of the pallium and their subdivisions. As discussed further in Chapter 30, the region labeled **Dp**, the **posterior zone of the dorsal pallium**, receives a major olfactory input. Whether it is a migrated part of the more proximal pallium or is a distal pallial component has not been resolved. Because it lies in close proximity to the hippocampal Dlv, it may provide olfactory information for spatial mapping and memory functions. Its medial part projects to the probable septal homologue, the ventral nucleus of area ventralis (Vv), but whether this projection resembles that of the hippocampal formation or the amygdala to the septal nuclei in amniotes is undetermined.

A number of ascending sensory pathways, including gustatory, mechanosensory lateral line, and auditory, are relayed to the telencephalon in teleosts through the preglomerular nuclear complex, a migrated group of the posterior tuberculum (see Chapter 20), rather than through the dorsal thalamus. Most of the ascending projections from the preglomerular nuclear complex are to the **medial zone of area dorsalis telencephali (Dm)**. In some electrosensory teleosts—specifically the ostariophysan catfishes and gymnotids—the preglomerular nuclear complex also relays ascending electrosensory information to Dm.

Part or all of Dm is a good candidate for a homologue of the pallial part of the mammalian amygdala, particularly the frontotemporal amygdala. Topologically, Dm lies in the corresponding location to the amniote pallial amygdala, i.e., in the most proximal part of the pallium. In amniotes, this location is in the ventrolateral-most part of the pallial hemisphere, juxtaposed to the striatum. Not only do the location and connections of Dm resemble those of the amniote amygdala, which are criteria for homology, but there are also indications of functional similarity. In amniotes, the pallial amygdala is essential for fear-conditioned responses to paired stimuli, such as presenting a light followed by a small electrical shock. The animal learns to associate the light with the anticipated shock, and both heart rate and respiration increase with presentation of

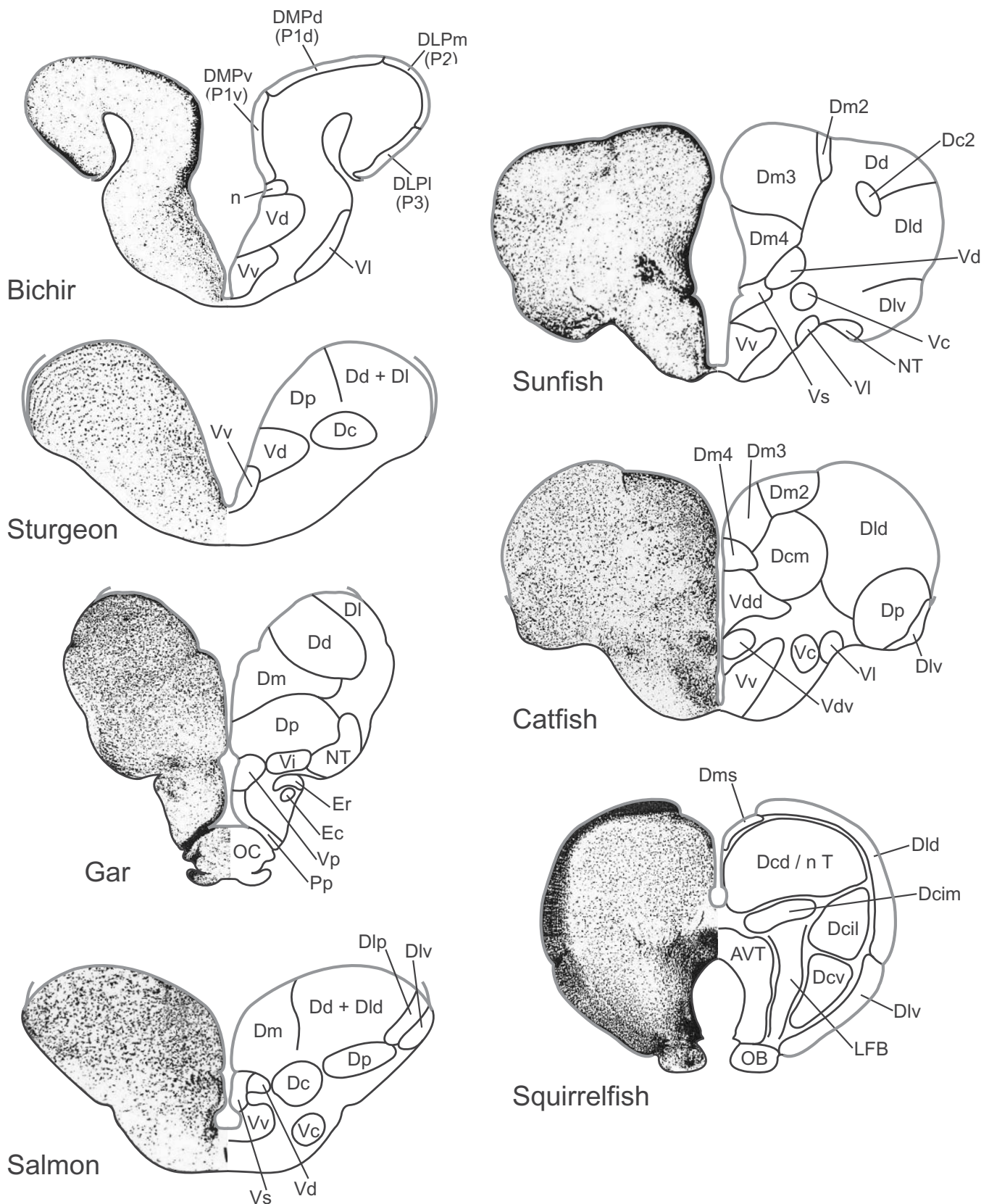


FIGURE 25-5. Transverse hemisections with mirror-image drawings through the telencephalons of various ray-finned fishes. The bichir (*Polypterus senegalus*, with pallial nomenclature after Holmes and Northcutt, 2003) and sturgeon (*Scaphirhynchus platyrhynchus*) represent basal radiations, whereas neopterygians are represented by the gar (*Lepisosteus osseus*) and the teleosts salmon (*Salmo gairdneri*), sunfish (*Lepomis cyanellus*) (the latter five figures after Northcutt and Braford, 1980), catfish (*Ictalurus punctatus*, after Striedter, 1991), and squirrelfish (*Holocentrus ascensionis*, after Demski and Beaver, 2001). The latter three species are euteleosts. In all cases, the ventricular surface is indicated by a gray line. The figures are used with the kind permission of Springer Science and Business Media (bichir, sturgeon, gar, salmon, and sunfish), John Wiley & Sons (catfish), and Spektrum Akademischer Verlag (squirrelfish).

the light itself. In goldfish, the same effect has been shown, and the integrity of Dm is necessary for it to occur. In contrast, lesions of the distal part of the hemisphere, the presumed hippocampus, do not affect the conditioned response or its acquisition. This work is discussed further in Box 30-1.

The **central zone of area dorsalis telencephali (Dc)** receives some ascending sensory inputs—particularly gustatory ones relayed through the preglomerular nuclear complex—as well as inputs from other pallial areas. It is also a major source of efferent connections of the telencephalon. Overall, the organization of the pallium in teleosts may consist of 1) a proximally lying Dm region that corresponds to the amniote pallial amygdala, including an olfactory amygdalar homologue ventrally (see Chapter 29) and the frontotemporal amygdala (which in amniotes receives collothalamoc inputs) dorsally, 2) a dorsal pallial region corresponding to the lemnopallial motor and visual areas of amniotes, and 3) a distal, lateral-most pallial region that corresponds to the amniote hippocampus. This arrangement is predicted by the simple eversion hypothesis with preservation of topology.

Behavioral Issues

As will be discussed in Chapter 28, the motor nuclei in the brainstem that are involved in communication behaviors have direct inputs from the telencephalon and the midbrain in birds and some mammals. In contrast, the possible roles of an elaborated telencephalon in Group IIA vertebrates for a number of complex behaviors, such as intraspecific communication, reproduction, feeding, and learning, for the most part remain to be explored. Among ray-finned fishes, parts of the telencephalon are known to be involved in the vocalizations of midshipmen fishes and in the electromotor system of gymnotids (see Chapter 12). Also, electrical stimulation of the preoptic area and of the supracommissural nucleus of the ventral telencephalon (Vs, see Fig. 30-8) is known to evoke acoustic communication signals in toadfishes. Toadfishes, which are closely related to midshipmen (see Fig. 12-5), produce such sounds by controlled contraction of sonic muscles in the lateral walls of the swim bladder. Additional studies are needed in fishes and amphibians on possible descending pathways, whether direct or multisynaptic, that could affect the output of the motor nuclei involved in producing communication signals. Other sound producing mechanisms used by various fishes include grinding of pharyngeal teeth and electric organ discharges. Amphibians use the larynx for vocalization. The motor nuclei controlling the production of communication signals variously receive input from the reticular formation and/or pacemaker nuclei in the medulla.

As discussed in Chapter 12, some of the supramedullary pathways involved in the control of electric discharges have been elucidated in gymnotid fishes. A diencephalic nucleus, nucleus electrosensorius, receives ascending electrosensory and octavolateral input and projects to multiple targets that include a nearby prepacemaker nucleus (Fig. 12-6). The prepacemaker nucleus is reciprocally connected with the ventral nucleus of area ventralis in the telencephalon, and it projects to the pacemaker nucleus in the medulla, which is involved in the control of the frequency of electric organ discharge.

Some other motor behavior patterns in anamniotes are related to mate selection or territorial defense, but forebrain projections that might be involved in the control of these behaviors, which are based on visual recognition and the response behaviors of conspecifics, remain to be explored. For example, some species of perciform teleost fishes—Siamese fighting fishes, paradise fishes, sunfishes, and various cichlids—erect their gill covers as part of a frontal display behavior during aggressive encounters with male conspecifics. The trigeminal motor nucleus, which controls the movement of the gill covers, is known to receive inputs from the reticular formation and other hindbrain sites. In addition, some other brainstem inputs to the reticular formation are known, such as those from octavolateralis nuclei. Possible descending telencephalic projections to these brainstem nuclei need to be investigated.

Teleosts have elaborate telencephalons with multiple migrated nuclear groups (Fig. 25-5). Involvement of some part of the telencephalic pallium in complex behavioral patterns has been demonstrated by using electrical stimulation. Stimulation of the telencephalic hemisphere evokes arousal and swimming behavior. Stimulation restricted to the medioventral part of the telencephalon produces feeding behavior, while stimulation of the dorsal central part (Dc) produces sweeping or nest building behaviors.

Some studies of learning have been done on various teleosts following surgical ablation of the telencephalon. In such cases, instrumental conditioning is impaired when the reinforcement is remote from the correct response. Avoidance learning tasks and successive reversal learning tasks are also severely impaired. Thus, the telencephalon in teleosts appears to play a significant role in some of the integrative functions necessary for learning. As referred to above and as will be discussed further in Chapter 30, a major breakthrough in understanding pallial function in teleosts has come from the work of Cosme Salas and his collaborators. The specifically hippocampal functions of spatial mapping and memory are subserved by the distal, ventrolateral part of the pallium (Dlv), while amygdalar functions of conditioned fear responses are supported by the dorsomedial pallium (Dm). These regions correspond topologically to where the hippocampal formation and amygdala, respectively, lie within the evaginated telencephalic hemispheres of amniotes. Additionally, the recent delineation of the fishunculi and motor eye fields in the motor region of the dorsal pallium will now allow further work to explore how these various pallial areas support complex motor behaviors.

THE NONLIMBIC PALLIUM IN AMNIOTES

Mammals: Neocortex

In mammals, the nonlimbic pallium consists of the neocortex (Fig. 25-6), which forms the bulk of the cerebral hemispheres. Its six-layered cytoarchitectural structure was discussed in Chapter 19. The neocortex can be divided into four major regions, or, in mammals with the higher brain-body ratios, lobes, as in humans and other primates. In primates (Fig. 25-7), the **occipital lobe** lies most caudally and includes the **primary visual cortex**, which is lemnothalamic-recipient,

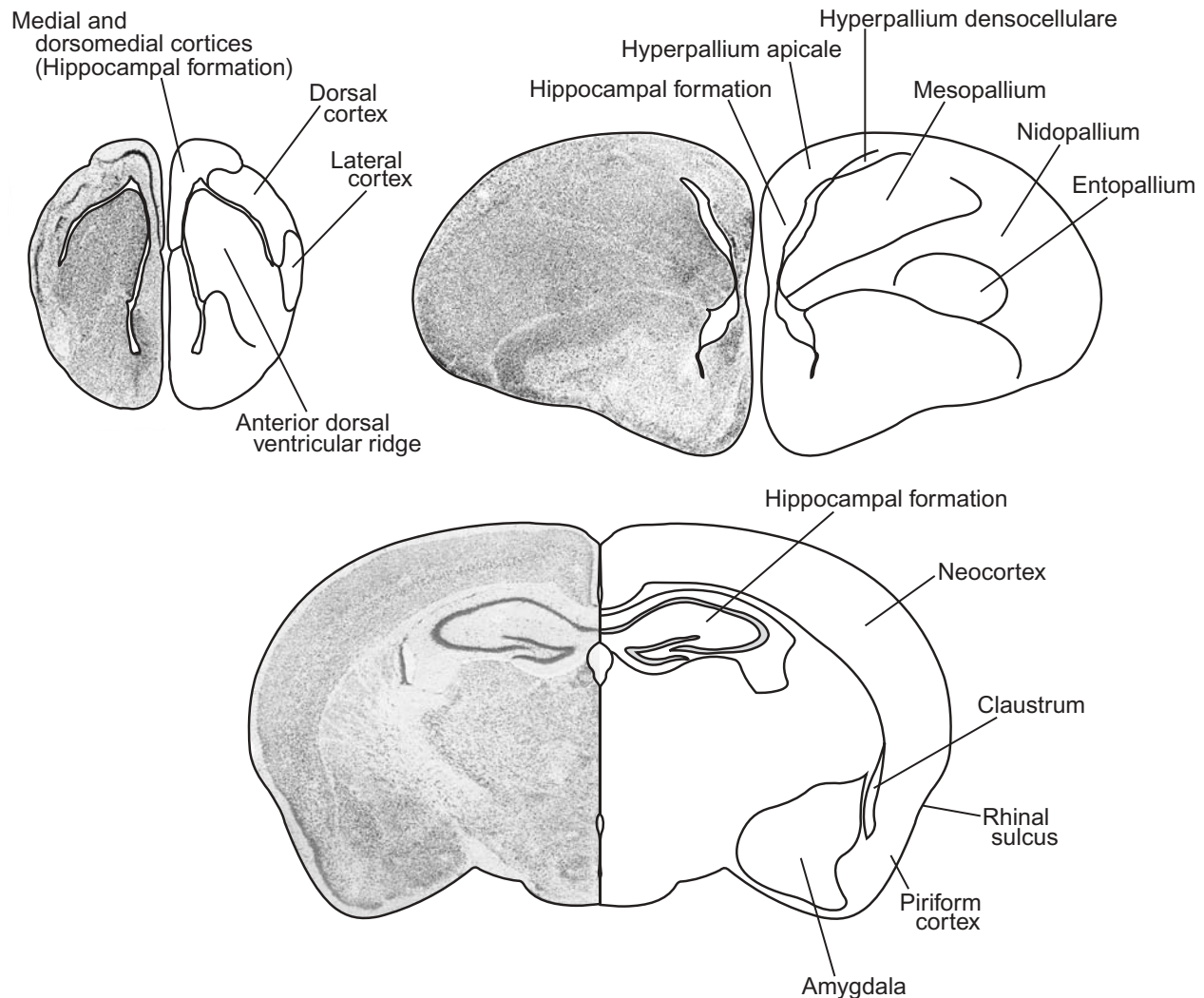


FIGURE 25-6. Transverse, Nissl-stained hemisections with mirror-image drawings through the telencephalon of the tegu lizard *Tupinambis nigropunctatus* (top left), the pigeon *Columba livia* (top right), and a mouse (bottom center). Pallial areas are labeled. Tegu lizard section from Ebbesson and Voneida (1969) and used with permission of S Karger AG, Basel. Pigeon section from Karten and Hodós (1967) and used with permission of The Johns Hopkins University Press. Mouse section from Slotnick and Leonard (1975).

and some of the collothalamo-recipient (secondary, tertiary, etc.) visual cortical areas. The **temporal** and **parietal lobes** lie rostral to the occipital lobe, with the parietal lobe situated dorsally and the temporal lobe more laterally and ventrally. The temporal lobe contains the cortical areas that receive ascending, collothalamo auditory pathways, including the **primary auditory cortex**, and the secondary, collothalamo somatosensory pathway as well. The parietal lobe contains the **posterior parietal cortex** caudally and the **primary somatosensory cortex** rostrally. The **frontal lobe** lies most rostrally. Its caudal part comprises the **primary motor cortex**, rostral to which lie **supplementary motor** and **premotor cortices**, and other, motor-related cortical areas. Rostral to all of the motor-related cortices is the **prefrontal cortex**. This brain region is characterized by a higher density of dopaminergic fiber innervation than other cortical regions

and also receives a projection from the mediodorsal nucleus of the thalamus. Both the prefrontal cortex and the posterior parietal cortex are involved in very high-level, integrative cognitive functions. In nonprimate mammals, such as rats (Fig. 25-8), similar divisions of the hemisphere are present, although the degree to which each is more or less elaborated and expanded varies considerably across the different orders of mammals.

The neocortex can be regarded as comprising two sets of cortical areas—one set consisting of the primary sensory-recipient and sensory association areas and the second set consisting of areas that are involved in high-level association and analysis functions. These sets of areas are fully interconnected along a continuum and have an extensive and overlapping network of reciprocal connections among themselves. We will briefly note the first set here, which will be covered in the next three chapters in much more detail, and then

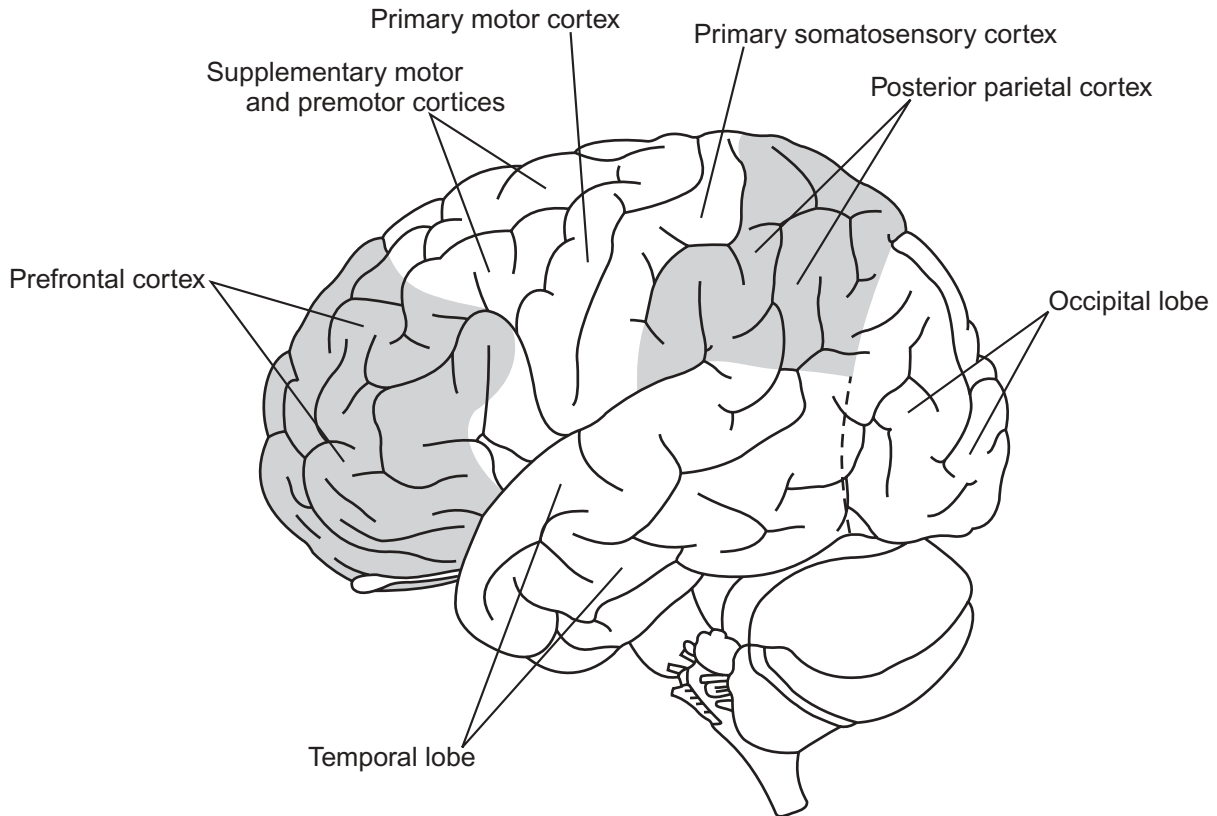


FIGURE 25-7. Lateral view of the brain of a human primate (*Homo sapiens*). Redrawn from Nieuwenhuys et al. (1978) and used with kind permission of Springer Science and Business Media.

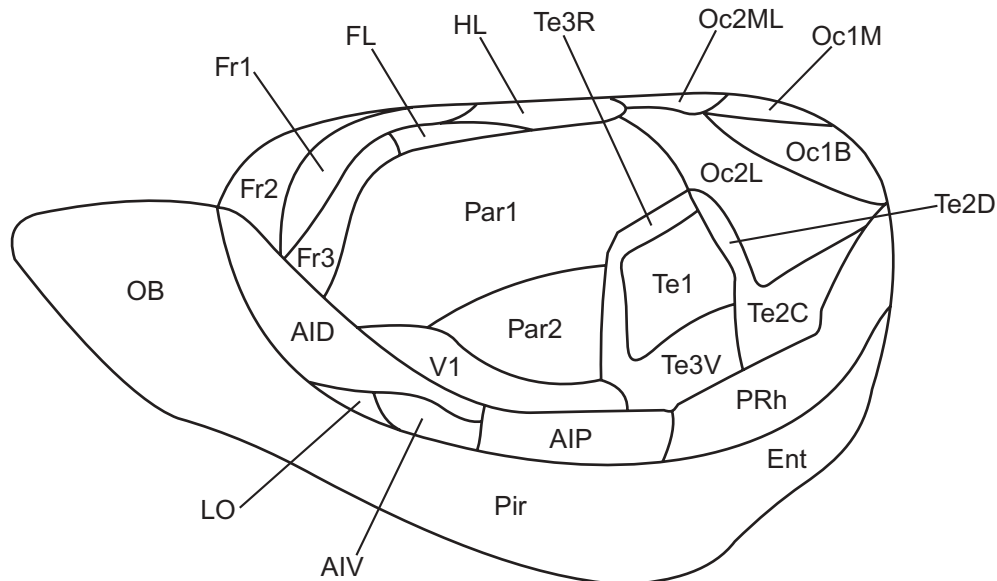


FIGURE 25-8. Lateral view of the brain of a rat. Redrawn from Zilles and Wree (1995) and used with permission of Elsevier. Abbreviations: AID, AIP, and AIV, agranular insular cortex, dorsal, posterior, and ventral parts; ENT, entorhinal cortex; FR, frontal areas; HL, hind limb area; LO, lateral orbital area; Par, parietal areas; Pir, piriform cortex; PRh, perirhinal cortex; OB, olfactory bulb; Oc, occipital areas; Te, temporal areas. Note that, in contrast to the human brain shown in Figure 25-7, the more ventrally lying, olfactory-related structures are visible from the lateral view.

discuss the major high-level cortical regions within the parietal and frontal lobes.

The primary visual cortex and some of the nearby collothalamo-recipient visual cortical areas of the occipital lobe can be regarded as sensory-recipient. They are involved in the receipt of the ascending sensory projections from the visual part of the thalamus and in rather extensive analysis of the information even at the initial cortical level. These areas are also highly interconnected in a reciprocal manner with the association visual cortical areas that extend from the occipital lobe far into the temporal lobe (for the visual stream dealing with fine form vision and color) and also into the association parts of the parietal lobe (for the visual stream dealing with location and motion). The evolution of these multiple visual cortical areas is discussed below in Box 25-1.

Similarly, the primary somatosensory cortex lies within the rostral part of the parietal lobe. It receives the ascending somatosensory inputs from the somatosensory thalamus and is highly interconnected with somatosensory association areas, including secondary and tertiary somatosensory cortices in the upper part of the temporal lobe and also the more posterior parts of the parietal lobe where the somatosensory information can be integrated with the visual information stream that deals with location and motion. Likewise, the auditory cortical areas of the temporal lobe receive the ascending auditory projections, participate in the initial cortical-level analysis of these inputs, and are then interconnected with auditory association cortices.

The association cortices of the parietal and frontal lobes support very complex cognitive functions, as discussed below in Box 25-2. These functions have been most thoroughly studied in humans and need to be noted here at least briefly for purposes of comparison with other mammals and other vertebrate taxa as well—particularly birds (see Box 25-3 below). The posterior part of the parietal lobe receives both somatosensory and visual information and is particularly concerned with spatial localization, as well as high-level functions such as attention.

The mediodorsal nucleus relays olfactory information to prefrontal cortex (Figs. 25-7 and 25-12). The role of a strong olfactory input to the prefrontal cortex in mammals is still somewhat enigmatic, as some mammals, such as primates, are generally considered to have reduced their use of the olfactory system in favor of other senses, particularly vision. Olfactory input may be more important than previously realized in both limbic and neocortical functions—including emotion, memory, learning, awareness of self, social interactions, mother-infant bonding, pheromones, and the set of distinctive behavioral characteristics unique to the individual.

The prefrontal cortex is also extensively interconnected with the posterior parietal cortex for its spatial information and with temporal association cortices for their visual form and color information. In humans, prefrontal cortex has been implicated as the site of many higher, conscious cortical functions and as being dysfunctional in disorders such as schizophrenia. The cortical area of the projection of the mediodorsal nucleus is also richly innervated by dopaminergic fibers that arise in the brainstem, and high levels of dopamine exacerbate schizophrenic symptoms. Among mammals, primates have an exceptionally large prefrontal cortical area. Intriguingly, echidnas also

have a very extensive prefrontal cortex but probably acquired this expansion independently.

Mammals: Claustrum-Endopiriform Formation and Frontotemporal Amygdala

In addition to the neocortex, the nonlimbic pallium (as we are defining it here) includes the claustrum-endopiriform formation and the frontotemporal amygdala. As discussed in Chapter 19, the claustrum-endopiriform formation comprises several pallial gray matter structures that lie dorsolateral to the amygdala and deep to the six layers of the overlying neocortex (Fig. 25-6). This formation is present in marsupial and placental mammals but whether any part of it is present in monotremes is a matter of debate. Subplate cells (see Chapter 3) persist into adulthood in some orders of mammals and essentially form a deep, or seventh, layer of neocortex. Where present, these layer VII cells are distinct from the claustrum and need to be separately distinguished.

The frontotemporal amygdala consists of two amygdalar nuclei, the **lateral nucleus** and the basolateral nucleus—specifically its anterior part, which we will refer to here as the **anterior basolateral nucleus**. The lateral nucleus of the amygdala is a ventral pallial derivative and is in direct receipt of the ascending collothalamo projections. The anterior basolateral nucleus is a lateral pallial derivative and receives projections from the lateral nucleus. Additionally, both of these nuclei have extensive reciprocal connections with cortical areas including those of the frontal and temporal lobes.

We need to qualify the designation of the mammalian basolateral amygdala as “nonlimbic,” which, in point of fact, is no more defensible than classifying it as limbic. The lateral nucleus of the amygdala is reciprocally connected with the hippocampus, specifically, its CA1 field (see Fig. 30-12, frontotemporal amygdala). The lateral and basal nuclei also project to entorhinal cortex. Thus, the frontotemporal amygdala clearly qualifies as a bona fide limbic system component. On the other hand, its receipt of ascending, collothalamo sensory projections and its interconnections with the frontal and temporal lobe cortices imply a more somatic nature. It is the latter attribute that we have chosen to emphasize by including it in this chapter.

Reptiles and Birds

The nonlimbic pallium in sauropsids consists of a dorsally lying structure—the **dorsal** (or general) **cortex** in reptiles and the **Wulst**, or **hyperpallium**, in birds—and the **dorsal ventricular ridge** (Fig. 25-6). The dorsal ventricular ridge, or **DVR**, consists of either a laminar cell plate with some centrally scattered cells or an enlarged area of nuclear groups. In our discussion of these areas, the nomenclature used for birds is that adopted by The Avian Brain Nomenclature Forum (see Tables 19-2–19-5).

In reptiles, the DVR is generally divided into an **anterior part**, the **ADVR**, which receives ascending collothalamo projections from various sensory systems, a **posterior part**, the **PDVR**, which receives projections from a variety of sources including the ADVR, and several other regions, one of which is the **nucleus sphericus**, which receives vomeronasal input (see Chapter 29). In birds, the DVR is considerably larger than

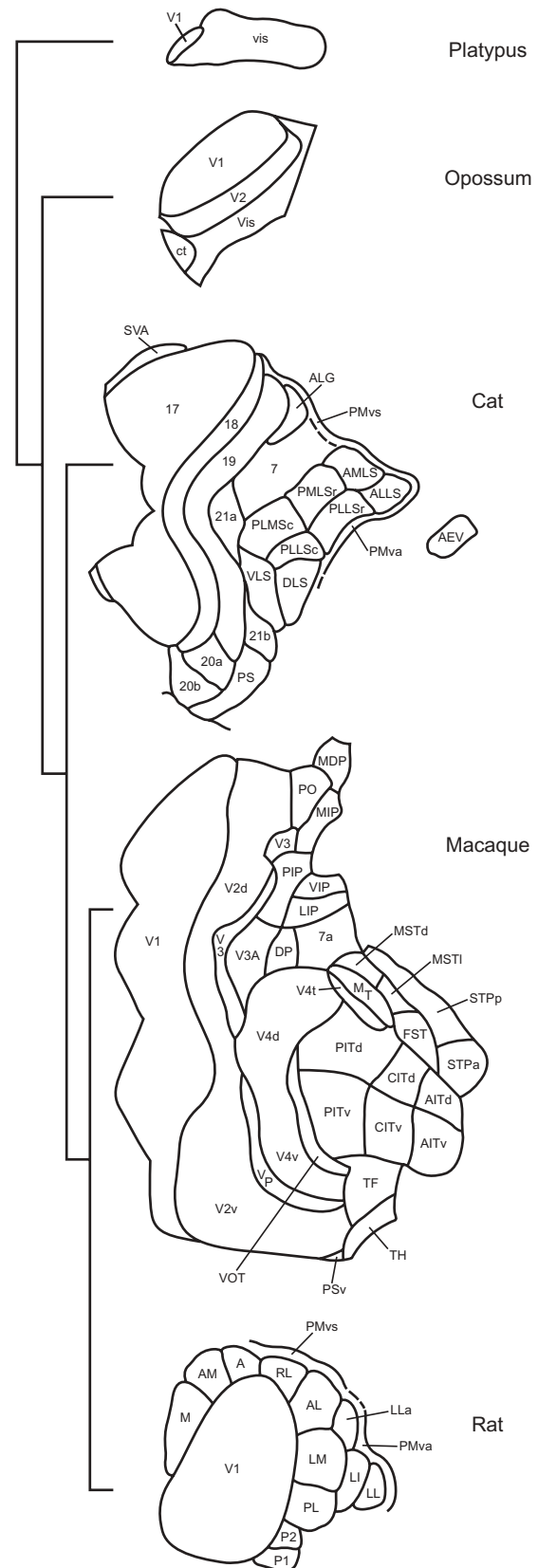
BOX 25-1. Evolution of Sensory Cortices Across Mammals

Different sets of sensory cortical areas—particularly the collothalamo-recipient cortices—have evolved independently in different orders of mammals. Although visual (V1, or area 17) and somatosensory (S1) lemnothalamo-recipient cortices show a very conservative evolution across mammals, collothalamo-recipient cortical areas have undergone dramatic changes, with multiple areas being gained independently in different orders. John Allman and Jon Kaas proposed that the additional cortical areas may have been added by a process of duplication of an existing area with subsequent adjustment of connections to produce a new area. Such a process would allow for the initially redundant, duplicated area to take on a new role in the analysis of sensory information.

As can be seen in Figure 1, the platypus, a monotreme, has a visual cortex that is tentatively identified as V1. A visual belt region is adjacent to the territory labeled V1, but additional visual cortical areas are not present. In the opossum, representing the marsupial radiation, several visual cortical areas are present, including the lemnothalamo-recipient V1 and several collothalamo-recipient areas, are present, but, as in the monotreme, the visual cortex is restricted to very few areas. In contrast, among the placental mammals, a plethora of collothalamo-recipient visual cortical areas have evolved multiple times. By way of example, the visual cortical areas of a cat are shown in the middle of the figure. Cats have many collothalamo-recipient visual cortical areas. The ones that lie most proximal to V1, such as 18 and 19, are most readily comparable to areas in other mammalian orders. However, the farther distally one goes in the hierarchy, the more unique areas are encountered that have no comparable counterpart in other orders.

In the macaque monkey map, a profusion of collothalamo-recipient visual cortical areas also are present, but those most distal to V1 are unique to the primate order. Even across primates, the collothalamo-recipient visual areas cannot all be compared one-to-one. Also, even though rats are more closely related to primates than are cats, the rat visual areas do not comprise nearly as many collothalamo-recipient ones as are present in primates. The many visual areas present in primates and cats have evolved independently within their separate orders. The somatosensory and auditory systems also have independently gained additional collothalamo-recipient cortical areas in different orders, although to a lesser extent than within the visual system.

FIGURE 1. Visual cortical areas mapped on a flattened surface in different mammals on cladogram from Fig. 4-13: platypus (Krubitzer and Huffman, 2000), opossum (Beck et al., 1996), and placentals (Sereno and Allman, 1991). Opossum drawing used with permission of John Wiley & Sons. Placental mammal drawings used with permission of Macmillan Press. Many of the visual cortical areas are identified here only by their abbreviations. The border of the area labeled vis in the platypus is approximate. Maps are not to the same scale.



BOX 25-1. Evolution of Sensory Cortices Across Mammals—cont'd

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BOX 25-2. Complex Cognitive Functions of Parietal and Prefrontal Cortical Areas in Humans

The prefrontal and parietal association cortices of humans and other primates (Fig. 25-7) support a number of highly complex cognitive activities. Only an exceedingly brief mention of their functions can be made here; however, because birds also have surprisingly complex cognitive abilities, these high-level functions need to be noted, and their relationship to the subjective experience of consciousness also needs to be mentioned. Specific cognitive abilities exhibited by birds and that require the same, high-level processing and capabilities are discussed in Box 25-3.

In humans, the posterior parietal cortex is involved in constructional features of stimuli, including a wide range of specific functions, as well as in the ability to fix and maintain attention. Its constructional functions include doing numerical calculations and being able to order spatial relationships. For example, persons with posterior parietal damage have difficulty in drawing pictures or diagrams with the correct spatial relationships. Such a person may also be unable to identify familiar objects by touch. The integration of visual and somatosensory stimuli in the spatial domain is disrupted.

The posterior parietal cortex is also essential, at least in humans, for being able to attend to the external world and to one's own body. Persons with damage to the left posterior parietal cortex do not suffer deficits of attention in this regard, but those with damage to the right posterior parietal cortex are unable to attend to the left side of the world and to the left side of their body. It is as if the left side of everything does not exist. The deficits include not grooming or dressing the left half of the body. In this regard, it is important to point out that rats and other small mammals, which have very little if any posterior parietal

cortex on either side of their brain, nevertheless groom both sides of their bodies and of course attend to stimuli in both sides of the external world. Likewise, birds groom and attend to stimuli bilaterally. Functions that are somewhat segregated in the human brain may thus be subserved by more "primary" cortical areas in other mammals or by non-cortical areas in nonmammalian vertebrates. This observation is a crucial one, since the presumption that high-level cognitive functions, including consciousness, are unique or mostly so to humans and other primates is a highly tenuous one.

The prefrontal cortex is the site of what have been termed "executive" functions, including making plans for the future, responding appropriately to social cues, being able to construct appropriate linguistic sequences, and working memory. The latter has been studied rather extensively, since a variety of behavioral measures can be used to test for it in humans as well as in nonhuman animals. As Joaquín Fuster points out, working memory is memory for the short term, as distinguished from "short-term memory" that is processed by the hippocampus (see Chapter 30) for consolidation into longer term memories held within the neocortex. As Fuster (2003) describes it, working memory is "an active and operant *state* of cortical memory." It is "*active memory* for the short term." He notes that it applies "to information held in the mind as needed for prospective action" and that the current, general meaning of this term can be used for nonhuman primates by dropping the constraint of human-level language. Episodic memory, which requires working memory, and is considered to be a very high-level, executive type of memory, also supported by the prefrontal cortex. It is autobiographical in that the

BOX 25-2. Complex Cognitive Functions of Parietal and Prefrontal Cortical Areas in Humans—cont'd

subject remembers not only a set of events but also remembers them in their proper temporal sequence and with proper spatial relationships. Fuster characterizes episodic memory as “the most heterarchical of all memories,” heterarchical referring to the combining of multiple hierarchical levels of sensory to high-level association processing networks. Episodic memories incorporate a wide range of memories, often including sensory, spatial, perceptual, emotional, and, in the case of humans, semantic.

Executive types of memory, such as working memory and episodic memory, which are supported by prefrontal cortex, generally are not considered to be unconscious processes. Definitions of consciousness vary, ranging from “simple” sensory awareness of stimuli to high-level, integrative experience. In his discussion of consciousness, Fuster posits that consciousness (beyond simple sensory awareness) “coincides with the temporary activation of its cortical network while it is being retained in working memory.” In fact, Bernard Baars has recently proposed that, rather than working memory being a necessary but possibly not sufficient prerequisite for the subjective experience of consciousness, working memory actually requires consciousness. By this argument, any animal that exhibits working memory should be given the benefit of the doubt as to being conscious.

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in reptiles, and more specific regions have been identified within it. As introduced in Chapter 19, the ADVL in birds comprises the **mesopallium** and a large region ventral to it, the **nidopallium**, which includes several sensory-recipient regions. More caudally is another part of the DVR, the **arcopallium**, which comprises some amygdalar components and other nuclei that are somatic in nature, i.e., their connections are not related to visceral, limbic, hypothalamic systems.

Ascending Sensory Pathways to the Pallium in Amniotes

The nonlimbic pallial regions of amniotes share a number of common organizational features, including the organization of afferent sensory pathways. These afferent pathways, which were introduced in Chapter 22, are summarized here. In the following three chapters (Chapters 26–28), the major visual, somatosensory-motor, and auditory regions of the telencephalon in amniotes will be discussed in detail.

Visual and Somatosensory Pathways: Lemnopallial. Two major visual pathways to the telencephalon are present in all amniotes and are shown diagrammatically for mammals and sauropsids (reptiles and birds) in Figure 25-9. In all amniotes, the lemnopallial pathway consists of projections from the retina to the dorsal lateral geniculate nucleus, which in turn projects to striate cortex in mammals and to a lateral part of dorsal cortex (or pallial thickening) in reptiles and the homologous part of the pallium, the visual Wulst, in birds.

The lemnopallial somatosensory pathway in mammals and sauropsids is shown in Figure 25-10. In mammals, the dorsal column nuclei project to the ventral posterolateral nucleus, which in turn projects to the primary somatosensory cortex. In sauropsids, the dorsal column nuclei project to the dorso-lateral part of the thalamus, and in birds specifically to a nucleus called dorsalis intermedialis ventralis anterior, or DIVA. The somatosensory information is then relayed to part of the dorsal cortex in reptiles and to the somatosensory part of the Wulst in birds.

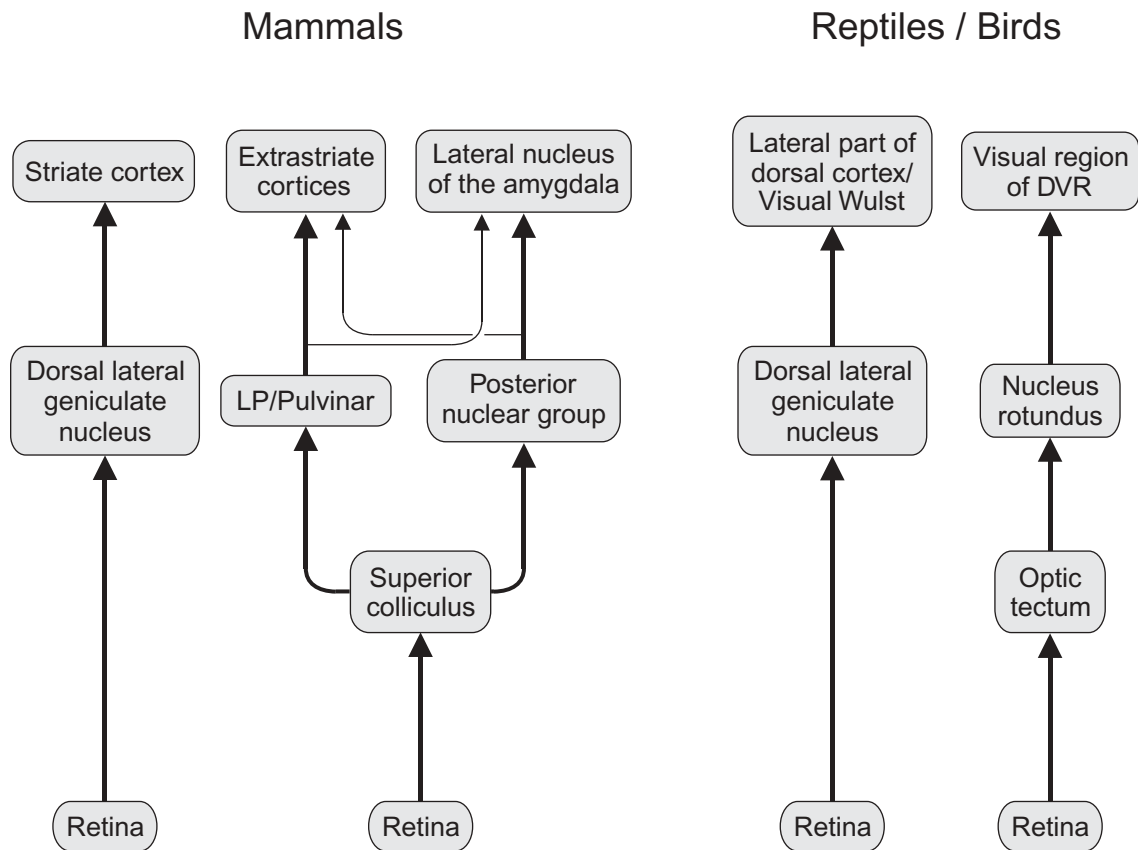


FIGURE 25-9. Diagram of visual pathways in mammals and sauropsids.

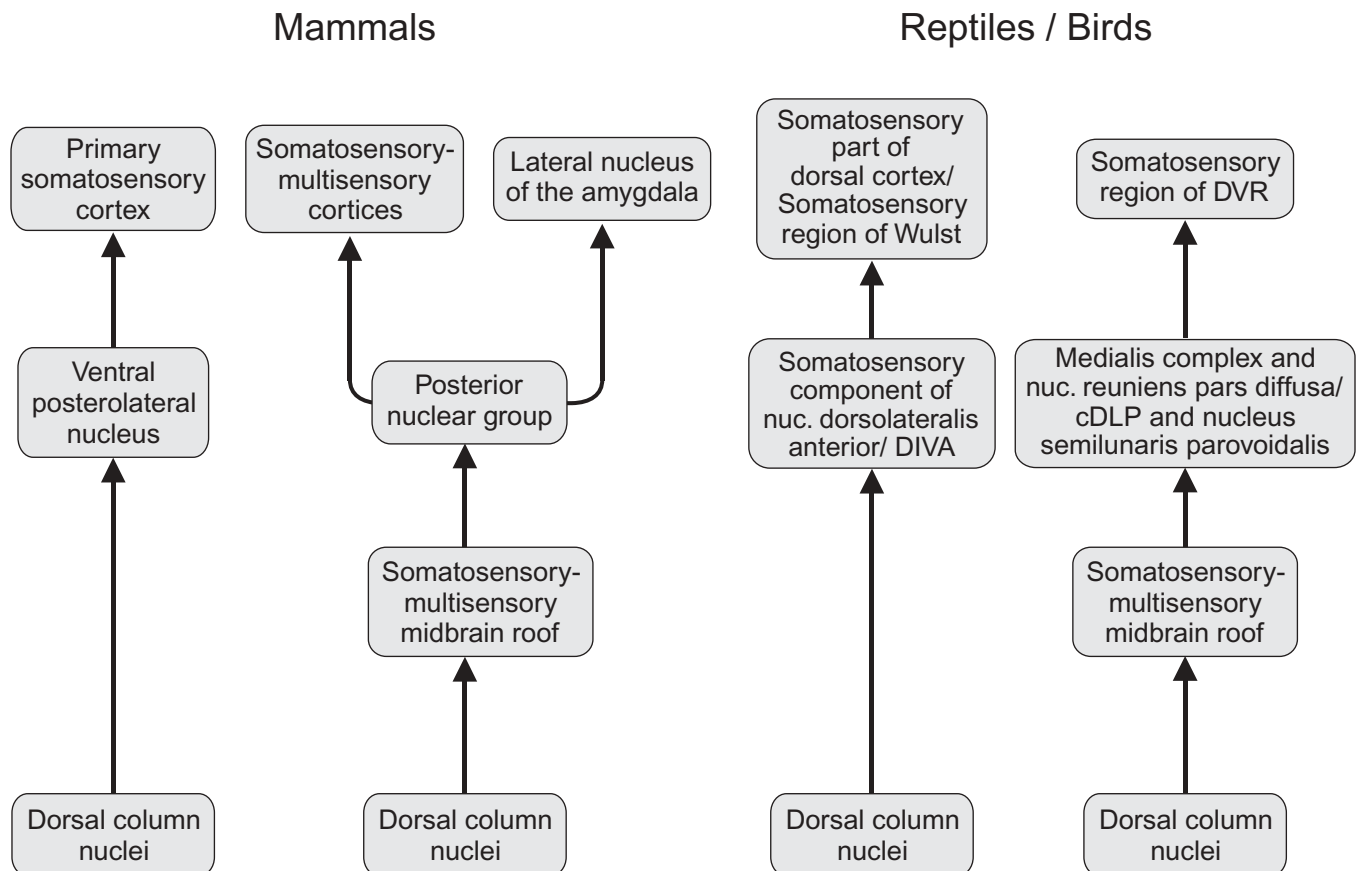


FIGURE 25-10. Diagram of somatosensory-multisensory pathways in mammals and sauropsids.

Visual and Somatosensory Pathways: Collopalial. In addition to projecting to the dorsal lateral geniculate nucleus in the dorsal thalamus, the retina also projects to the superior colliculus (optic tectum) in mammals and to the optic tectum in reptiles and birds (Fig. 25-9). In mammals, the superior colliculus projects to multiple dorsal thalamic nuclei, including two major sites, the lateral posterior/pulvinar complex (LP/pulvinar) and several nuclei within the posterior nuclear group. In reptiles, the optic tectum projects to only one major thalamic target, the large, centrally located nucleus rotundus. In birds, it projects to nucleus rotundus and additionally to the smaller and medially adjacent nucleus triangularis (not included in the figure). From the dorsal thalamus, projections are relayed to both the striatum and the pallium. In mammals, LP/pulvinar projects to the striatum and to extrastriate visual cortices, while the posterior nuclear group nuclei project to the striatum and also to the lateral nucleus of the amygdala. The distinction in pallial projection targets is not complete: LP/pulvinar gives rise to a minor projection to the lateral amygdala and the posterior nuclear group likewise to temporal lobe association visual cortices. In sauropsids, nucleus rotundus projects to the striatum and to one target within the pallium, a part of the anterior dorsal ventricular ridge (ADVR). In reptiles, this projection site does not have a specific name. In birds, it is called the entopallium. Like nucleus rotundus, nucleus triangularis also projects to the entopallium.

It should be pointed out that, in mammals, the segregation of the collothalamic and lemnothalamic pathways is not

absolute. The dorsal lateral geniculate nucleus gives rise to a minor projection to some of the extrastriate cortical areas, and LP/pulvinar projects lightly to striate cortex. As with tectal inputs to the thalamus, the lemnothalamic-collothalamic distinction is based on a predominance of the afferent and efferent projections rather than a completely separate and nonoverlapping pattern.

The collopalial somatosensory pathway (Fig. 25-10) begins with the relay of ascending sensory information from the dorsal column nuclei to the somatosensory part of the mid-brain tectum, i.e., the deeper layers of the optic tectum. The neurons within the deep layers of the optic tectum also receive visual inputs directly from the retina via the distal parts of their dendritic arborizations, as well as auditory inputs relayed rostrally from the inferior colliculus. This part of the tectum projects to the limitans-suprageniculate complex and the lateral part of the posterior nuclear group in mammals. It projects to the medialis complex and nucleus reuniens pars diffusa in reptiles and to a homologous pair of nuclei in birds, the caudal part of nucleus dorsolateralis posterior (cDLP) and nucleus semilunaris paravoidalis (Fig. 25-10). These collothalamic collothalamic nuclei project to an area of somatosensory-multisensory cortex and also to the lateral amygdaloid nucleus in mammals and to part of the dorsal ventricular ridge in birds.

Auditory Pathway: Collopalial. An ascending auditory pathway has been found in all amniotes and is shown diagrammatically in mammals and sauropsids in Fig. 25-11. The audi-

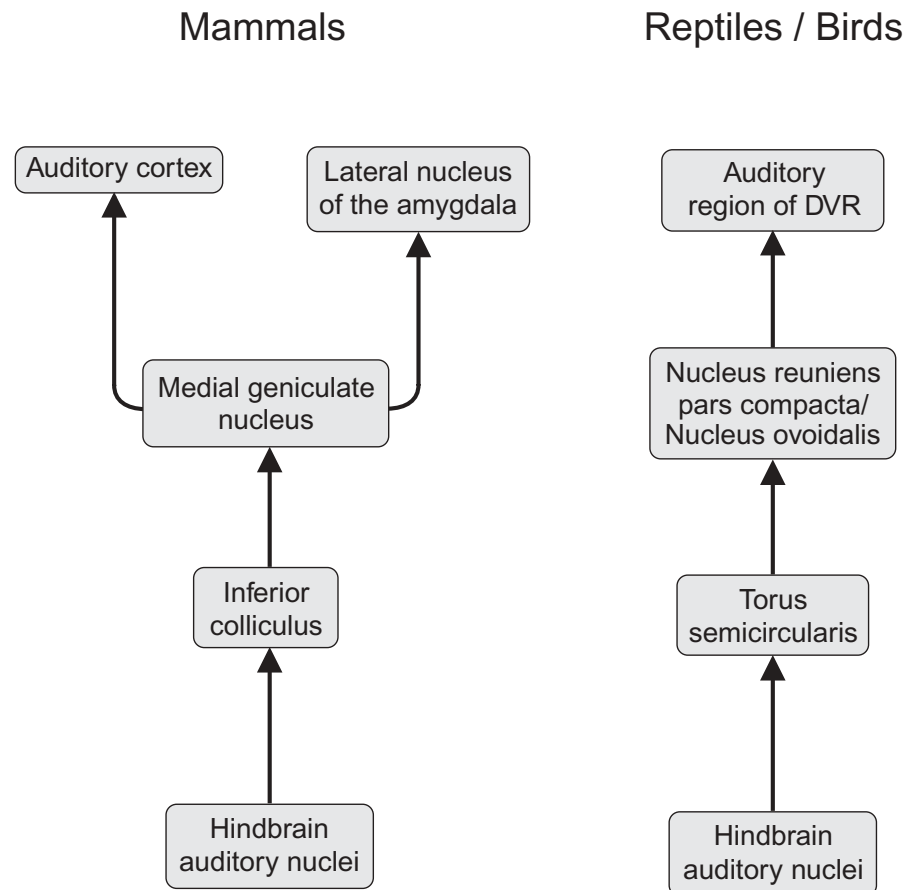


FIGURE 25-11. Diagram of auditory pathway in mammals and sauropsids.

tory part of the midbrain, the inferior colliculus in mammals and the torus semicircularis in sauropsids (also called nucleus mesencephalicus lateralis dorsalis, or MLd, in birds), projects to the dorsal thalamus—specifically to the medial geniculate nucleus in mammals and to a homologous nucleus in sauropsids, nucleus reuniens pars compacta in reptiles and nucleus ovoidalis in birds. This collothalamic nucleus projects to a part of the dorsal ventricular ridge in sauropsids, while different divisions of it project to the auditory cortex and to the lateral amygdaloid nucleus in mammals.

Olfactory Pathway: Lemnopalial. In mammals, an olfactory pathway (Fig. 25-12) is present from the olfactory cortex to the mediodorsal nucleus in the dorsal thalamus. The mediodorsal nucleus, a part of the lemnothalamus, projects to prefrontal and prelimbic cortical areas. The cortical terminal area of mediodorsal afferent fibers also is characterized by a large quantity of dopaminergic fibers that arise from the ventral tegmental area and substantia nigra of the midbrain. In birds, the olfactory cortex similarly projects to part of nucleus dorsomedialis (Fig. 25-12), which in turn projects to several parts of the pallium, including a caudally lying region called the dorsolateral corticoid area. A similar pathway has not yet been found in reptiles but, if present, would be expected to involve

the dorsomedial part of the dorsal thalamus and perhaps a caudal part of the dorsal cortex.

Other Afferent Pathways. The final major thalamopallial pathways that we need to note here arise from lemnothalamic nuclei and consist of the projections of the anterior, medial, and intralaminar nuclear groups in mammals and of the dorsomedial and anterior dorsolateral nuclei in nonsynapsid amniotes. In mammals, some of these nuclei project specifically to limbic and prelimbic cortices, including the subicular and hippocampal cortices, and some project diffusely to wide areas of the cortex. In nonsynapsid amniotes, the dorsomedial and anterior dorsolateral nuclei give rise to specific projections to the dorsal cortex as well as diffuse projections to wide areas of the dorsal cortex and dorsal ventricular ridge.

PALLIAL EVOLUTION AND PERSISTENT QUESTIONS OF HOMOLOGIES

The dorsal cortex and Wulst of sauropsids and their homology to the medial (i.e., lemnothalamic-recipient) part of neocortex is quite well established. These structures all receive ascending visual and somatosensory lemnothalamic projections, and, in both birds and mammals, they are known to give rise to descending motor projections, including a pyramidal tract that projects directly to the spinal cord. A marked difference exists, however, in the cytoarchitecture in terms of what cellular territories are generated from particular portions of the ventricular zone. Loreta Medina and Anton Reiner used glial patterns and other indicators to determine that the so-called layers of the avian Wulst are not oriented in the same way as the layers of neocortex. In fact, they essentially lie in an orthogonal orientation (Fig. 25-13). In mammals, within any radially oriented unit, all six layers of neocortex are present, germinated from the same locus of the ventricular zone. In birds, however, each radially oriented unit contains only the equivalent of one component of cortical layers, such as layer IV-equivalent cells alone in IHA (the interstitial part of the hyperpallium apicale), where the thalamopallial fibers from the dorsal lateral geniculate nucleus terminate. Medina and Reiner thus suggested that the “layers” of the Wulst are better regarded as “**pseudolayers**.”

This radial alignment of cortical layer-equivalent neuron populations in the Wulst is also supported by recent findings of gene expression patterns in birds and mammals by Jennifer Dugas-Ford and Clifton Ragsdale. A gene expressed specifically in layer IV of neocortex is also expressed specifically within IHA but not within other pseudolayers of the Wulst. Not all neocortical neuronal components, as identified by their neurotransmitter histochemistry, are present in reptiles, however; some have been gained independently in birds and mammals (see Chapter 19). New neuronal phenotypes, particularly the granule cells of the main thalamic-recipient layers of sensory cortices, layers II and IV, appeared in the synapsid line in conjunction with the gain of the inside-in migration pattern during the development of the cortex. Some dorsal pallial neuronal populations with neurotransmitter phenotypes similar to

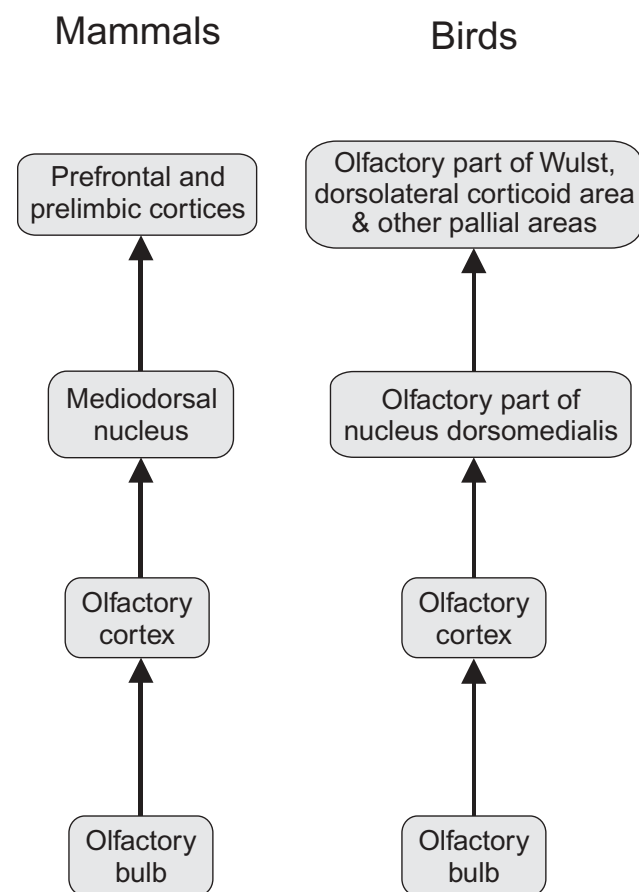


FIGURE 25-12. Diagram of olfactory dorsal thalamic pathway in mammals and birds.

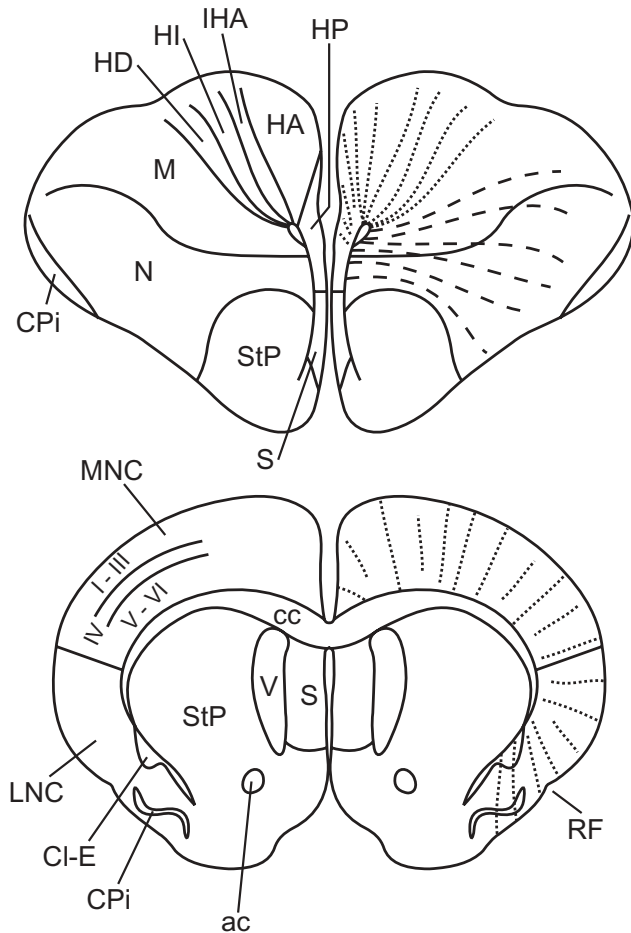


FIGURE 25-13. Top: drawing of a transverse section through the brain of the pigeon (*Columba livia*) showing pseudolayers in the Wulst, based on Medina and Reiner (2000) and indicated by dotted lines, and probably similar histodevelopmental strata in the dorsal ventricular ridge, based on Striedter and Beydler (1997) and indicated by dashed lines. Medina and Reiner drawing adapted with permission of Elsevier. Bottom: similar drawing of a rat telencephalon showing the radial glial orientation, indicated by dotted lines on the right side, versus the horizontal laminar structure of the neocortex, indicated on the left side. Cortical layers are indicated by the Roman numerals. Abbreviations for pigeon brain: CPI, piriform cortex; HA, hyperpallium apicale; HD, hyperpallium densocellulare; HI, hyperpallium intercalatum; HP, hippocampus; IHA, interstitial part of hyperpallium apicale; M, mesopallium; N, nidopallium; S, septal nuclei; StP, striatopallidum. Abbreviations for rat brain: ac, anterior commissure; cc, corpus callosum; Cl-E, claustrorodentiform formation; CPI, piriform cortex; LNC, lateral (collopallial) part of neocortex; MNC, medial (lemnopallial) part of neocortex; RF, rhinal fissure; S, septal nuclei; StP, striatopallidum; V, lateral ventricle.

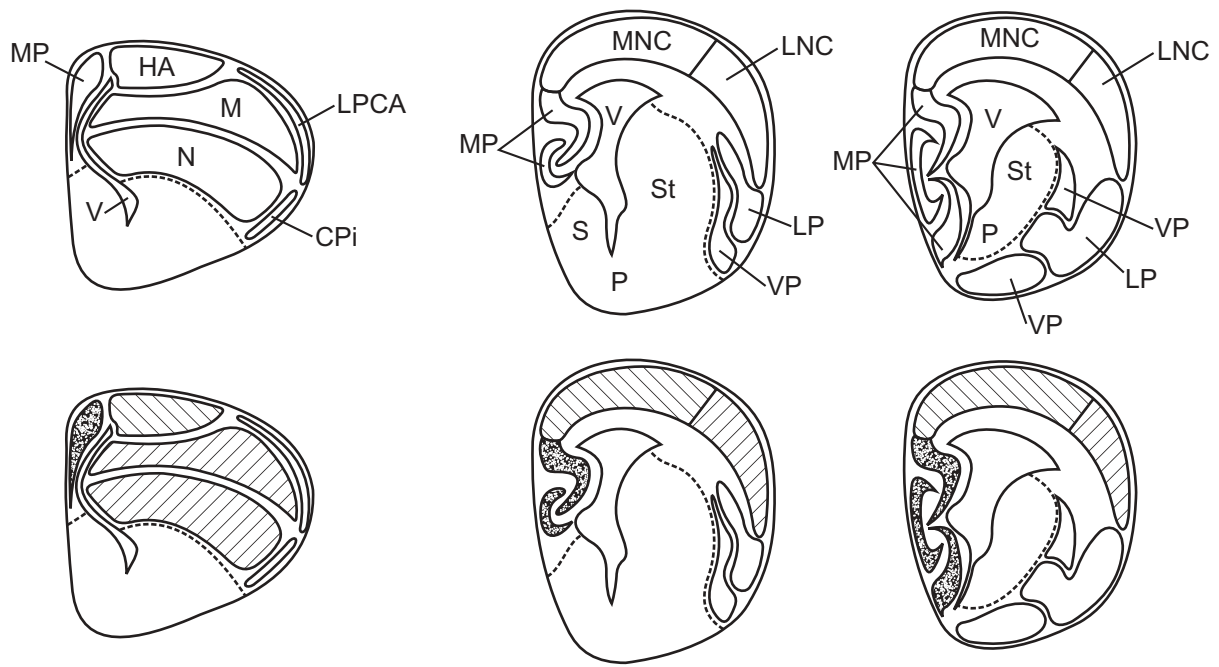
those in layers II–IV of mammalian neocortex are also present in birds, such as those identified by gene expression in IHA. Whether such neurons are also present in the dorsal cortex of reptiles needs to be tested with genetic markers.

In contrast to the situation with the lemnopallial Wulst/dorsal cortex of sauropsids, proposed homologies of

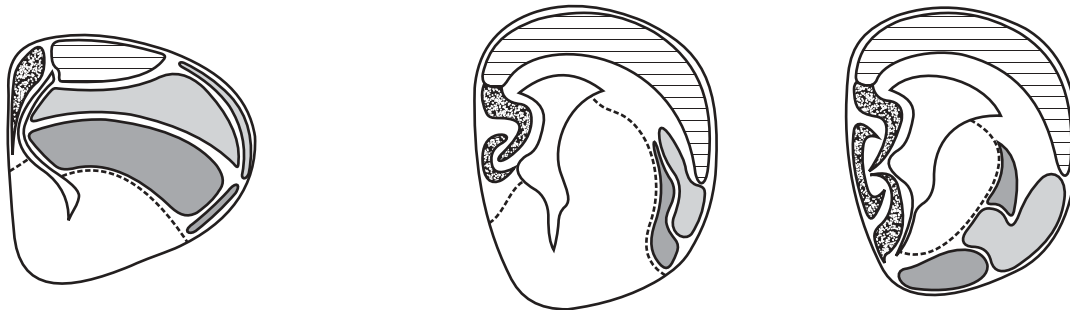
mammalian collopallial components to those of sauropsids vary considerably, as summarized in Chapter 6 and in Figure 25-14. In reptiles, particularly lizards, the ADVR has been posited as the homologue of the lateral (collothalamic-recipient) part of mammalian neocortex, of the lateral amygdalar nucleus, or of both of these entities as a field homology. Others have posited that the ADVR is independently evolved in the sauropsid line and is not comparable to any pallial structure in mammals; instead, the PDVR is proposed as the homologue of the mammalian lateral amygdalar nucleus (and several related structures). The PDVR is a multisensory region, receiving visual, auditory and somatosensory inputs from the separate sensory fields within the ADVR as well as relayed main olfactory and vomeronasal inputs, and it projects to the ventromedial part of the hypothalamus. Along with this alternate proposal of the PDVR corresponding to the lateral nucleus of the amygdala, a dorsolateral part of the DVR, called the **dorsolateral amygdala (DLA)**, is proposed as the homologue of the mammalian anterior basolateral amygdalar nucleus. DLA receives relayed main olfactory and vomeronasal inputs, and it projects to the dorsal striatum and nucleus accumbens.

In birds as in reptiles, the ADVR—the mesopallium and nidopallium—have been compared to the lateral (collopallial-recipient) part of mammalian neocortex, the lateral amygdalar nucleus, or both as a field homology. The region previously called archistriatum has been recently divided (by The Avian Brain Nomenclature Forum) into two divisions, one entirely pallial part called arcopallium and another partly pallial, partly subpallial part given names that include the term amygdala. The entirely pallial part includes several nuclei, one of which is the nucleus robustus arcopallii as present in songbirds (see Chapter 28). The rest of the arcopallium consists of nuclei that either give rise to commissural projections or contribute the majority of fibers that form a major descending tract, the **occipitomesencephalic tract**. This tract carries arcopallial projections to multiple brainstem targets, including dorsal thalamus, medial spiriform nucleus, midbrain roof, and reticular formation. However, it does not carry fibers that terminate with limbic-associated targets, such as the hypothalamus or the central core of the brainstem. Due to this pattern of projections, Hans Zeier and Harvey Karten recognized in 1971 that the part of the arcopallium that gives rise to the occipitomesencephalic tract is somatic rather than limbic in nature. The recently designated term “arcopallium” was chosen for its neutrality, since the possible relationship of this region to any part of the pallium in mammals is presently unclear.

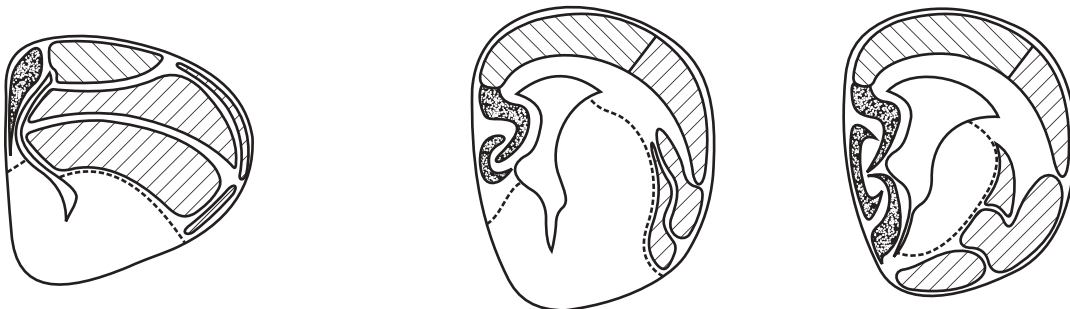
The amygdalar components—i.e., limbic part of the caudolateral avian pallial region and—now recognized by that name in birds—comprise three cell groups: the posterior pallial amygdala area, nucleus taeniae amygdalae, and area subpallialis amygdalae or subpallial area. The latter two nuclei appear to correspond to the medial and extended amygdalar components in mammals and were discussed in Chapter 24. The **posterior pallial amygdala** (previously two cell groups called the pars ventralis of the ventral archistriatum and the posterior archistriatum) contributes a minor contingent of fibers to the occipitomesencephalic tract, but its main efferent target is the hypothalamus. It is the latter attribute that identifies it as an amygdalar structure. Further work needs to be done to clarify the relationships between the arcopallial and amygdalar



Karten (1969), Reiner (1993, 2000), Butler (1994)



Bruce & Neary (1995), Puelles et al. (2000)



Butler and Molnár (2002)

FIGURE 25-14. Overview of three current theories on the evolution of the dorsal pallium in amniotes. Diagrammatic representations based on Puelles (personal communication.) In each row, a drawing of a transverse hemisection through the telencephalon of a developing bird is shown to the left, and two drawings of transverse hemisections through the telencephalon of a developing mammal are shown to the right, with the far right drawing being the more caudal one and through the level of the amygdala. In the top row, the structures are identified. The second row illustrates the ADVR-lateral neocortex hypothesis of Reiner (1993) and Butler (1994b), derived from the equivalent cell hypothesis of Karten (1969). The third row illustrates the ADVR-claustroamygdalar hypothesis, variations of which are supported by Bruce and Neary (1995), Striedter (1997), Puelles and his co-workers (Puelles et al., 2000; Puelles, 2001; Medina et al., 2005a,b), and Martínez-García et al. (2002). The fourth row illustrates the ADVR-lateral neocortex plus claustroamygdalar field homology hypothesis of Butler and Molnár (2002). Shading and fill patterns are used to indicate comparative structures for each hypothesis. Since the piriform cortex is not shown as a separate entity in the mammalian figures but rather is included in the LP/VP regions, it is not shaded in most cases. All of these hypotheses basically agree on a discrete homology of most or all of piriform cortex across amniotes. Abbreviations as in Figure 25-13 and: LP, lateral pallium; LPCA, lateral pallial cortical area; MP, medial pallium; P, pallidum; St, striatum; VP, ventral pallium.

components of birds with pallial components in both reptiles and mammals.

Whatever the homologies of pallial areas in mammals and sauropsids, the most compelling questions have to do with function and how diverse neural substrates can support similar, highly complex cognitive abilities. As discussed below in Box 25-3, the cognitive abilities of birds are as extensive as they are varied. Birds arguably have more and higher-level cognitive skills than most mammals, and these abilities are supported by the pallial areas in the telencephalon—the Wulst and dorsal ventricular ridge. The architecture of both the individual neuronal dendritic forms and the arrangement of the neurons with respect to each other differ markedly between birds and mammals, however. As Terez Tömböl and her co-workers as well as others have demonstrated, most of the neurons in the dorsal ventricular ridge and also in the Wulst have dendrites that radiate in a star-shaped array. Their geometry is thus quite different from that of the pyramidal neurons of neocortex,

which have a radially oriented apical dendrite and much shorter basal dendritic arborizations. Although pyramidal and bipyramidal neurons are present in the avian hippocampal formation (see Chapter 30), only a minority of neurons in the rest of the avian pallium show a pyramidal cell-like apical dendrite with a polarized orientation.

While neuronal architecture is conspicuously different, similarities of circuitry—in terms of the ascending pathways as discussed above and in terms of loops from the pallium through the striatopallidum and dorsal thalamus and then back to the pallium (see Chapter 24)—are striking. This shared circuitry thus may be one of the crucial neural features that support the complex cognitive abilities of both mammals and birds.

A particular area in the caudal part of the pallium has been identified in birds as either homologous and/or analogous to mammalian prefrontal cortex. This pallial area is called the **nidopallium caudolaterale**, NCL (Fig. 25-15), or caudolateral

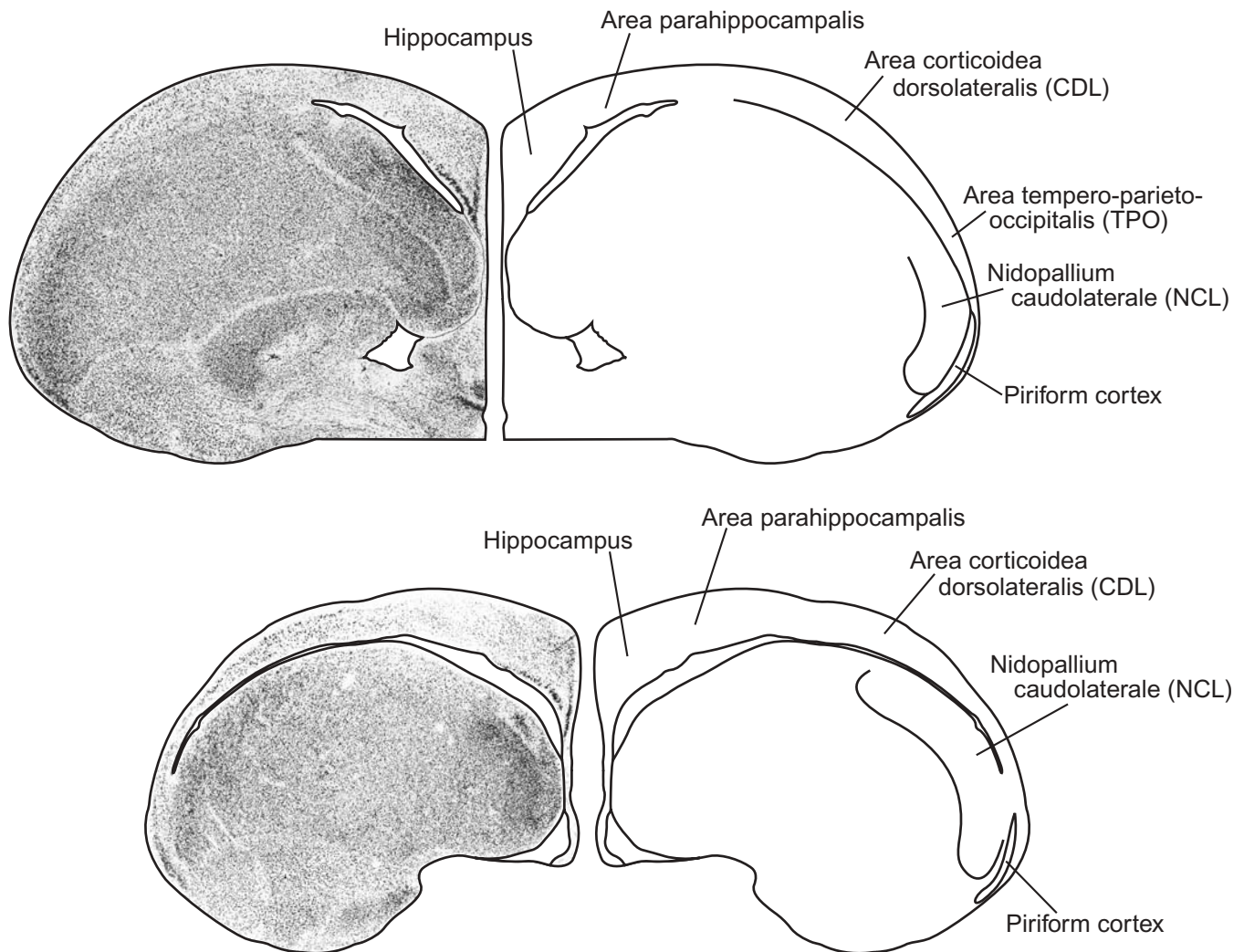


FIGURE 25-15. Transverse Nissl-stained hemisections with mirror-image drawings through the telencephalon of the pigeon (*Columba livia*). The more rostral section is at the top. Adapted from Karten and Hodós (1967) and used with permission of The Johns Hopkins University Press.

nidopallium (formerly the caudolateral neostriatum). It was initially identified as a possible homologue of prefrontal cortex by Ivan Divac, based on its particularly rich dopaminergic innervation. Divac and his co-workers carried out a number of anatomical and behavioral studies, which have been extended substantially by Onur Güntürkün and his co-workers. Like prefrontal cortex, NCL is reciprocally connected with sensory pallial areas—the visual, auditory, and somatosensory regions of the nidopallium. NCL also receives an input from the Wulst. Unlike the prefrontal cortex however, which receives a lemnthalamic input, NCL receives ascending multisensory information relayed through a collothalamic nucleus, the nucleus dorsolateralis posterior. Efferents of NCL include projections to the striatum and also to the somatic part of the arcopallium and the posterior pallial amygdala. Lesions of NCL cause deficits in a variety of behavioral tasks that require high-level cognitive abilities, such as working memory tasks and reversal learning. For these types of tasks, previously learned information has to be compared with current sensory inputs for the correct response choice to be made. As discussed above in Box 25-2, working memory tasks are highly dependent on the prefrontal cortex in humans and other mammals.

Another nearby part of the pallium, the more dorsally lying region called the **area corticoidea dorsolateralis**, **CDL** (Fig. 25-15) or dorsolateral corticoid area, has been proposed as an alternate best candidate for a prefrontal cortex homologue. Andras Csillag and his co-workers noted that this region, which blends into NCL ventrolaterally, receives inputs from the lemnthalamic dorsomedial thalamic nucleus (as shown in Fig. 25-12), which receives olfactory inputs from piriform cortex. The olfactory-recipient part of this nucleus is thus an excellent candidate for a homologue of the mediodorsal nucleus of mammals on both topographical and connectional grounds. The mediodorsal nucleus projects to prefrontal cortex, while the dorsomedial thalamic nucleus of birds projects to several pallial sites, including the dorsolateral corticoid area. Since the dorsomedial nucleus also projects to the Wulst, the possibility of a prefrontal cortex homologue in that region cannot be ruled out for the present time. The behavioral deficits seen with lesions of NCL, some of which invariably involve the overlying CDL, point to one or both of these caudal pallial regions as the most likely candidates. A neighboring pallial region called the **temporo-parieto-occipital area**, or **TPO**, is also of interest in this regard and remains to be systematically examined for its possible contributions to complex cognitive functions.

BOX 25-3. The Impressive Cognitive Abilities of Birds

The term “birdbrain” is often used in a pejorative sense to insult someone’s intellect. The substantial body of information now available on the impressive cognitive abilities of birds contradicts this folk notion. Whatever the specific homologous relationships between nonlimbic pallial regions in mammals and sauropsids turn out to be, there is no doubt that birds have achieved a very high cognitive level. This level of ability is in keeping with their brain-body ratios, which comfortably overlap those of mammals, even slightly overlapping the primate level in some species (Fig. 1).

Birds are capable of many cognitive abilities previously thought to be only the province of mammals, primates, or even humans and to be particularly supported by the prefrontal and posterior parietal cortical areas (see Box 25-2). These abilities include reversal learning and delayed matching-to-sample tasks, transitive inference, multistability of ambiguous figures, episodic memory, object constancy, substantial linguistic and numerological abilities, complex category formation, and tool manufacture. Birds also may exhibit theory of mind: scrub jays appear capable of attributing the potential of their own possible future actions to a conspecific. The questionably “higher” ability to spontaneously lie in order to maintain the normal access to a reward, similar to primate behavior in some situations, also has been demonstrated. It is thus compellingly clear that the cognitive abilities of birds are on a par with those of most mammals, certainly including primates.

In this regard, it is important to note a point that Joaquín Fuster makes in his book on *Cortex and Mind*. Delay tasks are commonly used to test working memory in humans and other primates. However, studies in nonhuman animals that involve creating lesions in particular brain areas and then testing with various delay paradigms have shown that prefrontal cortex is not essential for learning to perform to criterion on these tests. Criterion on delay tasks can be achieved after destruction of the prefrontal cortex, but it is achieved only after extensive training, with many more trials than the normal, intact animal would require. In the studies discussed here on birds, excessively long training periods are not required, indicating that their functional capabilities—whatever the neural substrate—are indeed on a par with those of intact, normal primates.

As discussed above, the caudolateral nidopallium, or NCL, has been proposed as the equivalent of mammalian prefrontal cortex. Lesions of this region in birds result in deficits in tasks that require working memory. For example, a delayed matching-to-sample task, or DMTS, can be designed for pigeons by presenting keys that can be pecked in order to gain a reward, which usually consists of access to a feed tray for a short period of time. For the DMTS task, the pigeon pecks the middle key of three, which is illuminated with either a red or a green light, then waits through a delay period with no key illuminated, and then is asked to peck one of the two laterally lying keys illuminated with the matching color rather than the other lateral key illumi-

BOX 25-3. The Impressive Cognitive Abilities of Birds—cont'd

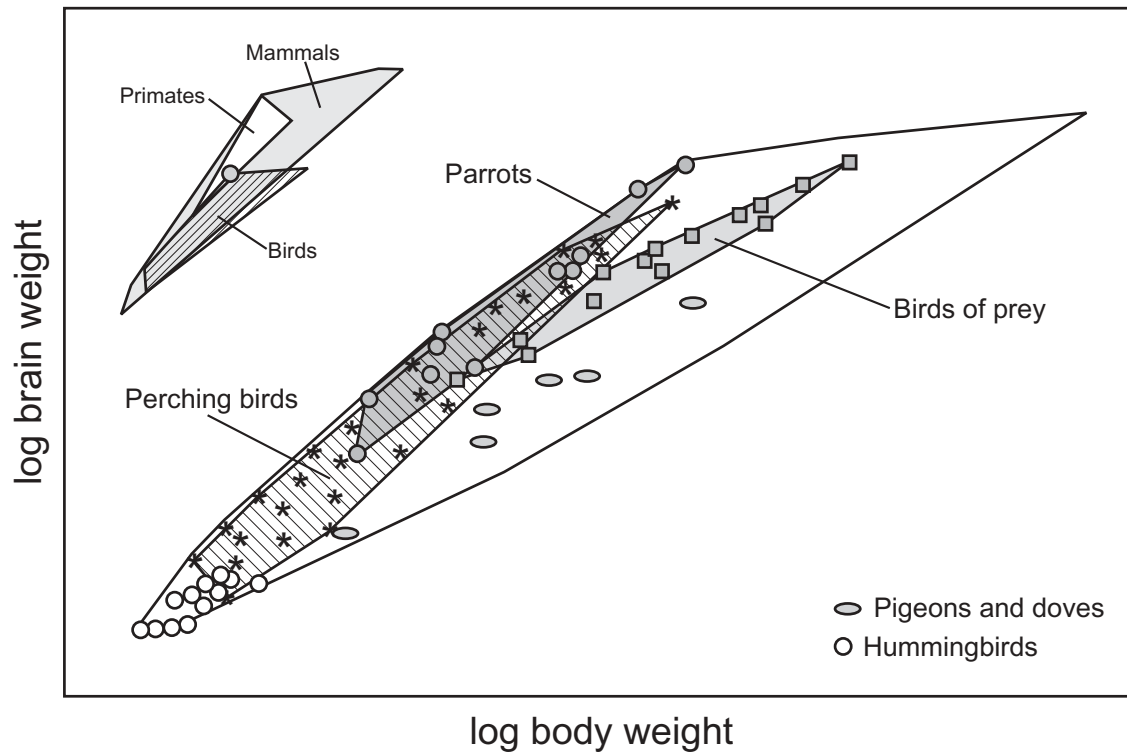


FIGURE 1. Log brain weight plotted as a function of log body weight for a number of species of birds. The geometrical figures are the minimum convex polygons that enclose all of the data points for the entire taxon. Among birds, data are shown for perching birds, or passerines (hatched polygon and asterisks), which include songbirds, pigeons and doves (gray ovals), hummingbirds (white circles), birds of prey (lighter gray polygon and gray squares), and parrots (darker gray polygon and gray circles). The latter exhibit the highest brain-body ratios for birds and even overlap the primate range, as indicated by the gray circle on the inset, which compares the overall minimum convex polygon (hatched) of birds with that of mammals (gray) and within mammals, primates (white). Data points that lie along the long axis of each polygon represent species that have a brain weight that would be expected from their body weight. Those at the top of the polygon have brain weights that are greater than would be expected from their body weights. Conversely, those at the bottom of the polygon have lower than expected brain weights. Thus, among birds, pigeons and doves, which exhibit markedly good cognitive abilities, have brain weights that fall along the predicted line for their body weights as compared with other birds, whereas perching birds, which include songbirds, birds of prey, and parrots all have larger brains than would be expected from their body weights alone. Data on birds adapted from Nieuwenhuys et al. (1998) and that on mammals from Jerison (1973).

nated with the other color. Such tasks are considered to test for working memory, since the brain must keep the memory of the stimulus key “on-line” in order to compare it with the test keys when they are illuminated after the delay period. Normal pigeons can do this task successfully, but those with lesions of NCL cannot.

Many such high-level cognitive abilities have been demonstrated in pigeons, which have brain-body ratios that fall within the middle range for birds (Fig. 1). For example,

pigeons are capable of transitive inference, which refers to the ability to infer relationships or other features of stimuli from a set of data. Pigeons also show evidence of having mental expectations based on their responses to ambiguous figures. The phenomenon of multistability of ambiguous figures, also called coherence, has been considered unique to primates and to be a function of working memory, thus involving prefrontal cortex. This phenomenon implies the existence of a mental expectation and is exemplified by

BOX 25-3. The Impressive Cognitive Abilities of Birds—cont'd

drawings, such as the Necker cube (the familiar 3-dimensional line drawing of a cube), that can be perceived as in one or another configuration but never as both configurations simultaneously. The neural basis for such perceptions may be related to that which supports the perception of illusory contours, which in owls has been identified as the visual Wulst. Electrophysiological recordings from single neurons have demonstrated that a high proportion of the visual Wulst neurons respond specifically to subjective illusory contours, just as neurons in mammalian visual cortices do.

Episodic memory is another example of such a highly cognitive function once thought to be unique to humans but apparently within the repertoire of jays, who are members of the corvid (crow) taxon and thus have some of the highest levels of brain-body ratios among birds (Fig. 1). Nicola Clayton and her colleagues demonstrated apparent episodic memory in scrub jays for the location, content, and the relative time since food items were cached. Even more remarkably, Clayton's laboratory studied cache behavior in these birds that implies theory of mind, which is the attribution of one's own mental experiences to another, including the idea that a conspecific might do what oneself would do under similar circumstances. In this experiment, individual jays were first given an opportunity to cache food items when clearly being observed by a conspecific. The jay was then allowed to return to the cache site in private. Jays who themselves had not previously stolen from the caches of other jays did not change the location of their own caches. In contrast, jays that had previously stolen from other jays changed the location of their caches. Thus, rather than being the unique province of primates, the rarified level of cognitive ability that supports theory of mind may also be shared by some birds. Both episodic memory and theory of mind are supported by prefrontal cortex in mammals; evidence for these abilities in jays thus suggests involvement of such pallial regions as the NCL and/or the CDL in the caudal part of the telencephalon.

In regard to communication, a number of songbirds share the rare trait of vocal learning, a behavioral substrate for spoken human language (Brenowitz, 1997). A substantial body of literature has been amassed on the vocal circuitry in birds, as will be discussed in Chapter 28. Among birds, African gray parrots are outstanding for their verbal abilities. Irene Pepperberg's remarkable work with Alex and other African gray parrots has established that these birds have substantial linguistic and numerical abilities. Alex's semantic and quantitative skills are extensive and remarkable, in keeping with the very high brain-body ratios for parrots, which overlap the lower end of the primate range (Fig. 1).

The body of work on the cognitive abilities of birds is broad and extensive enough to establish that they are capable of high-level cognitive processing. Their abilities include those briefly discussed here as well as additional

ones that in mammals also are associated with the prefrontal cortex and working memory, such as Piagetian object constancy, category formation and discrimination, and tool use and manufacture. As noted above, the nidopallium caudolaterale and/or the dorsolateral corticoid area appear to be similar in function to the prefrontal cortex of mammals, particularly primates. These regions within the caudal part of the pallium along with the neighboring temporo-parieto-occipital area and also the more dedicated sensory regions such as the Wulst are thus prime candidates for the neural basis for such abilities in birds. Although the pallium of birds is organized in very different cytoarchitectonic configurations than the pallium of mammals, it is clearly capable of supporting these complex cognitive processes. The key features of similarity that underlie the shared functional capacities may be more in the circuitry than in the cytoarchitecture. While the latter is markedly different, birds and mammals share many features of forebrain circuitry, involving dorsal thalamic nuclei, dorsal and ventral striatopallidum, and pallial areas. It is beyond the scope of this book to discuss in more detail the cognitive literature on birds, but we have included a number of references in the list below that the interested reader can delve into.

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BOX 25-3. The Impressive Cognitive Abilities of Birds—cont'd

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Visual Forebrain in Amniotes

INTRODUCTION

A fox stealthily moves through the tall grass of a meadow in search of a meal. A noise somewhat to his left attracts his attention. The large, sound-gathering pinnae of his ears localize the source; his eyes and head reflexively turn to this point in space. Something is moving there. The fox fixates both eyes in the direction of the sound source. The image of a ground squirrel comes into focus on the fox's retina. So too does the image of the tall grass in front of the squirrel as well as images of the earth, twigs, and leaves behind the squirrel. The fox's visual system must sort out this jumble of lines, textures, colors, and shapes to present the fox with a representation of the critical features of its visual environment. The target must be sharply differentiated from the foreground and the background. Other factors need to be evaluated: How far away is it? Is this something to pounce on for an easy meal? Or is it something that is too big to handle? Is it something with formidable defenses like a porcupine or snake? Or is it something that might make a meal of the fox? Finally, the fox must consider what the consequences were of his last encounter with something that looked like that. The neuron populations in the fox's visual system perform these and related analyses continuously as the fox moves through the visual world.

In previous chapters, we discussed the visual system at the receptor level and at the levels of the midbrain and thalamus. We pointed out that the tectum of the midbrain is a region that permits the central nervous system to coordinate "maps" of the body with "maps" of the surrounding sensory worlds of vision, hearing, and some other distance senses. These midbrain maps allow for our fox's eyes and head to orient accurately toward

the source of the sound. Information about other properties of the external visual world is sent to the dorsal thalamus directly from the retina via the optic nerve and tract. From the dorsal thalamus, visual pathways ascend to the telencephalon, which processes the visual information that will be used to guide the fox's decisions.

Much of our understanding of the visual forebrain comes from the study of mammals. Until the last several decades, the mammalian pattern of thalamic nuclei and telencephalic areas was regarded as a unique achievement of mammals. Comparative anatomists and physiologists now recognize that the mammalian pattern also exists in reptiles and birds and indeed has certain features in common with amphibians, cartilaginous fishes, and ray-finned fishes as well. A unifying framework for discussion of these features is provided by the concept of dual ascending sensory pathways to the dorsal thalamus, the lemnothalamic and collothamic pathways, which we discussed in Chapters 19, 22, and 25. The lemnothalamic pathways bring sensory information for various systems to the dorsal thalamus directly (i.e., without a synapse in the midbrain roof) from the spinal cord, brainstem, and retina. The collothamic pathways also carry sensory information to the dorsal thalamus from the spinal cord, brainstem, and retina, but they do so via the midbrain roof, which is known as the colliculi or the tectum in mammals and the tectum in nonmammals.

Both the collothamic and lemnothalamic nuclei send their efferents to separate areas of the pallium in the telencephalon. In mammals, these areas are the **frontotemporal division of the amygdala** (see Chapters 19 and 25) and various parts of the **sensory neocortex**. The presence of thick granule cell layers (II and IV) is one of the hallmarks of sensory cortex. The axons of the dorsal thalamic neurons terminate in

the granule cell layers of the sensory cortical areas, predominantly in layer IV (see Chapter 25). In this chapter, we will explore the visual pathways to the telencephalon and their regions of termination.

IPSI LATERAL RETINAL PATHWAYS AND STEREOSCOPIC VISION

The typical relationship between the retina and the brain in vertebrates is for each retina to send most of its axons to the contralateral half of the brain. Thus, the right eye sends its **optic nerve** across the midline to the left side of the brain. The place where the two optic nerves cross is known as the **optic chiasm**. The term “chiasm” is derived from the Greek word for the crossing of two lines, as in the Greek letter *chi*, which has the same shape as our letter X. For most vertebrates, the vast majority of optic axons project to the contralateral side of the brain, although some ipsilateral axons have been reported in many vertebrates. In mammals, however, the situation is somewhat different; considerable numbers of retinal axons do not cross but enter the brain on the same side. One theory of the heavy contralateral termination of optic axons holds that this crossing is related to the right-left reversal (as well as inversion) of the images of objects when they pass through the optics of the eye and form on the retina.

The marked increase in the percentage of ipsilateral retinal axons in some mammals may be a consequence of a shift in the location of the eyes from a more lateral position in the skull to a more frontal position. In general, the more frontal the location of the eyes, the greater is the proportion of ipsilateral retinal axons. In rodents, which have relatively laterally located eyes, the ipsilateral retinal axons are approximately 10% of the total number. In carnivores and primates, which have frontal eyes, the ipsilateral retinal axons are in the range of 40–50% of the total retinal projection to the brain.

Frontally located eyes have **binocular vision**, i.e., there is a considerable degree of overlap in the regions of visual space that each eye can survey. If the extent of overlap is suf-

ficient, it permits the development of **stereoscopic** (three-dimensional) **vision**, which offers the animal a highly precise estimate of the distances of objects. Such ability is of enormous advantage to predators, which must accurately assess the distance of prey for the final assault. Stereoscopic vision is also of value to animals that are not typically predators—animals that have become adapted to life in the trees, such as squirrels, tree shrews, and primates. Accurate determination of distance is vital for life in the arboreal environment as the animal moves from branch to branch, sometimes executing feats of acrobatics, as well as for gathering food. Similar considerations apply to the diurnal bats that make use of vision rather than echolocation when foraging for food.

VISUAL PATHWAYS TO THE TELEENCEPHALON IN MAMMALS

Lemnothalamic Visual Forebrain

The visual lemnothalamic route is from the ganglion cell layer of the retina (see Chapter 2) to its target cell population in the dorsal thalamus. The mammalian term for this structure is **nucleus geniculatus lateralis, pars dorsalis**, which translates as the dorsal part (or division) of the lateral geniculate nucleus or, more simply, the **dorsal lateral geniculate nucleus**. This structure may have a greater number of acceptable abbreviations than any other structure in the brain; they include, but are not limited to LGN, GLD, DLGN, DLG, GLd, or LGd. (Take your pick!)

The word “geniculate” comes from the Latin word *genu*, which means a “knee” and refers to the knee-like appearance of this structure in humans and other primates. The modifier “lateral” serves to distinguish it from the medial geniculate nucleus, which is an auditory dorsal thalamic relay nucleus. The similarity of names and the close proximity of the two nuclei are unfortunate, however, because it suggests to beginners that the medial geniculate nucleus is the auditory equivalent of the dorsal lateral geniculate nucleus. As discussed in greater detail

BOX 26-1. Evolution of the Skull and Evolution of Frontal Vision

Animals that are predators tend to have frontal vision that predisposes the animal to the retinal disparities that lead to stereoscopic vision, which is a powerful advantage in judging the distance to the prey. Prey animals, such as rabbits, have lateral eyes, sometimes located high on the skull. These favor the development of panoramic vision, which is 360° scanning of the visual world without moving the eyes or head.

The shift of the location of the eyes in the skull necessary for frontal vision appears to have begun in the therapsid ancestors of mammals. The shift may have occurred as a consequence of the enlargement of the **zygomatic arch** of the skull. The zygomatic arch is a bony arc formed

by three bones of the skull of mammals. Under this arc passes the **temporalis muscle**, which is one of the major muscles that close the jaw. The space under the zygomatic arch through which this masticatory muscle passes is known as the **temporal opening**, which is the single fenestration in the skull by which mammals are classified as synapsids (see Chapter 4). The chewing of food (rather than just swallowing it whole or in large chunks) and the resultant increased efficiency of food-resource utilization are characteristics that have only evolved fully in mammals, allowed for by the increased development of the zygomatic arch and temporalis muscle. In addition, the structure of the skull changed, permitting greater mechanical strength to with-

BOX 26-1. Evolution of the Skull and Evolution of Frontal Vision—cont'd

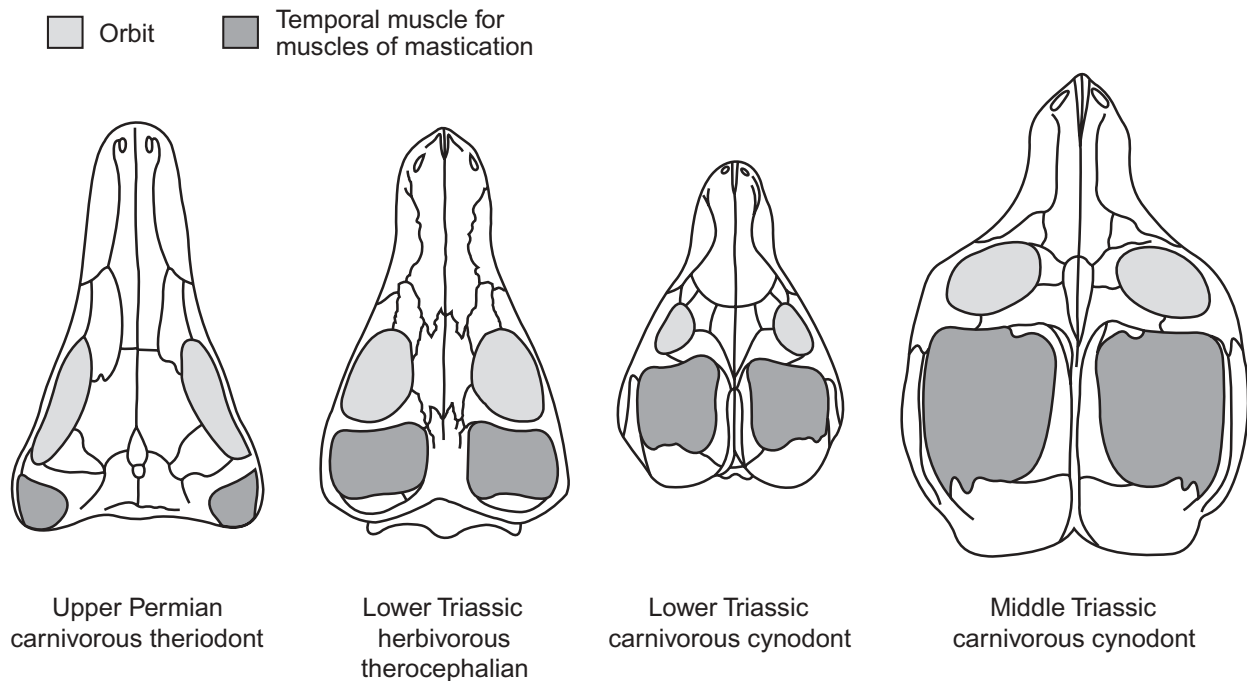


FIGURE 1. Drawings of skulls of four synapsids to show the relationship between the development of the muscles used for chewing, the zygomatic arch (the arc of bone that surrounds the temporal opening), and the shift from lateral to frontal orbits. The Upper Permian carnivorous theriodont has distinctly lateral orbits, small muscles of mastication, and a small temporal opening. The Lower Triassic herbivorous therocephalian and Lower Triassic carnivorous cynodont, later forms of that shown to left, have more frontal orbits, larger muscles of mastication, larger temporal openings, and larger zygomatic arches. The Middle Triassic carnivorous cynodont, similar to the lower Triassic carnivore, has distinctly frontal eyes, massive muscles of mastication, large temporal openings, and a large zygomatic arch. From Carroll (1988) and used with permission of Henry Holt & Company.

stand the enormously increased stresses that were placed on the skull due to the greater pull of the increasingly more powerful muscles. With the enlargement of the zygomatic arch and strengthening of the skull, the **orbits** (eye sockets) were pushed forward to the front of the skull and closer to the midline especially in the carnivorous orders of early mammals.

Figure 1 shows skulls that represent four stages in the evolution of the therapsid skull. These animals vary in their use of jaws for chewing and also in the location of the orbits in the skull. In this figure, the early therapsid from the late Permian era shows the typical early amniote pattern of a small zygomatic arch and small temporal openings through which the temporalis muscle passed en route to the lower jaw. This skull also has orbits that are located in a lateral position. In the two Lower Triassic animals, one herbivorous and one carnivorous, enlarged temporal openings are present,

and the orbits are located more frontally. The Lower and Middle Triassic carnivores show the pattern that is typical of modern carnivores, primates, and other frontal-eyed mammals, that is, a large zygomatic arch, large temporal openings, and frontally located orbits.

As may be seen in Figure 2, the shift to frontal eyes resulted in a greater overlap of the visual fields of each eye, producing a large binocular field, which in turn set the stage for the development of effective stereoscopic vision, which is vision in three dimensions. In general, the greater the degree of overlap, the greater the distance over which stereoscopic vision is functional. One should note, however, that as Figure 1 suggests, the shift of the orbits to the front and toward the midline may not have been driven by selective pressures related to vision but rather by selective pressures related to feeding. Once in their new location, however, the relatively few ipsilateral retinal axons now

BOX 26-1. Evolution of the Skull and Evolution of Frontal Vision—cont'd

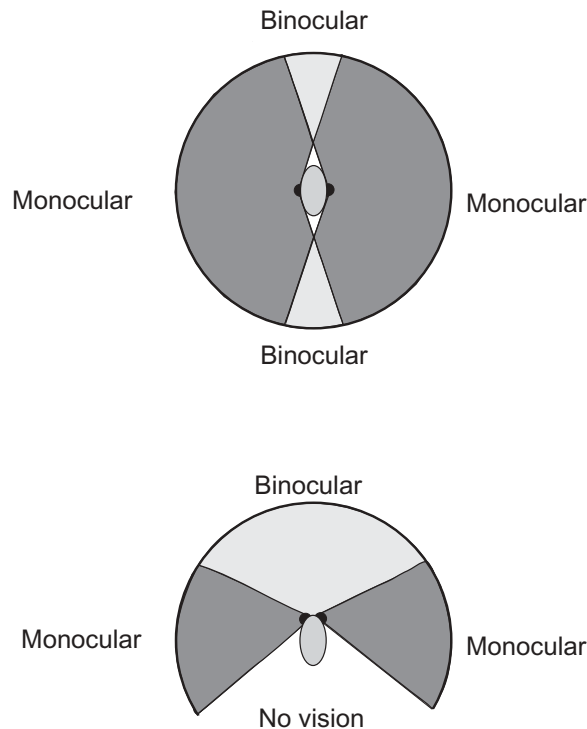


FIGURE 2. Diagram of the effects of a shift from lateral orbits to frontal orbits on the size and location of the monocular and binocular visual fields. Top: a mammal with lateral eyes has panoramic vision, a small field of binocular overlap in the front, another small binocular field in the back, and large monocular fields at the sides. Bottom: a mammal with frontal orbits has a large binocular field in the front, moderate monocular fields at the sides, and no vision in a substantial sector of the visual field at the rear.

took on a more important role, and a new set of selective pressures on the visual system came into operation, affecting a new evolutionary trend toward greater representation of the ipsilateral retinal fields.

Figure 2 also illustrates the point that only predators, or those with a low risk of predation because they are adapted for life in the trees, can afford the luxury of stereoscopic vision; the price paid for frontal eyes is the loss of panoramic (360°) vision, which is an effective early warning system for the approach of predators from the rear.

The shift to more frontal eyes among mammalian predators and primates, and the consequent increase in ipsilateral retinal input to the brain, had a profound impact on the evolution of the mammalian central visual system. At the dorsal thalamic level, it is correlated with an elaborate organization of the visual lemnothalamus into laminae that are organized to maintain segregation of ipsilateral and contralateral inputs and that contain functional channels that are organized according to the laminae. With this arrangement, visual information coming from each eye is kept separate until it reaches the level of the neocortex where interaction then permits the fusion of the two retinal images, resulting in the perception of the three dimensionality of objects and of visual space.

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in Chapter 28, the two are quite different; the dorsal lateral geniculate nucleus is a lemnothalamic nucleus, whereas the medial geniculate nucleus is a collothalamus nucleus.

In mammals, the pars dorsalis of the lateral geniculate nucleus is composed of two or more subdivisions. Of these subdivisions, some receive the ipsilateral retinal axons, and the others receive the contralateral retinal axons. In mammals with laterally located eyes, such as many ground-dwelling rodents, rabbits, and eulipotyphlans (previously called insectivores: see Chapter 4), the dorsal lateral geniculate nucleus consists of a single aggregation of cells in the caudal dorsal thalamus. The axons of the ipsilateral and contralateral components of the **optic tract** (the name for the bundle of retinal axons after they pass the optic chiasm) terminate in separate regions within this aggregation, with the contralateral segment being the larger in many nonprimate species. The locations of the ipsilateral and contralateral termination fields can only be determined experimentally by chemically or otherwise labeling the axons that follow each route. The distributions of labeled and unlabeled

axons sometimes reveal a “covert” or hidden segregation pattern. Moreover, in some mammals, such as rats and opossums, segregation of the ipsilateral and contralateral retinal axons is incomplete; that is, the ipsilateral and contralateral axons terminate in overlapping fields. In mammals with frontal eyes, such as tree shrews, carnivores, and primates, the dorsal lateral geniculate nucleus consists of a number of plate-like layers or **laminae**. In primates, in which the proportion of ipsilateral and contralateral axons approximates 50%, the pattern of lamination consists of equal numbers of ipsilateral and contralateral layers.

Figure 26-1 is a schematic representation of the two eyes and their respective visual fields of a mammal. An arrow is shown in the visual field; the image that each part of the arrow forms on the right and left retina is shown within the drawing of the right and left eye. The figure further shows the terminations of the ganglion cells of the right and left retinas in the right and left lateral geniculate nuclei. The right and left optic nerves are also shown emerging from their respective retinas.

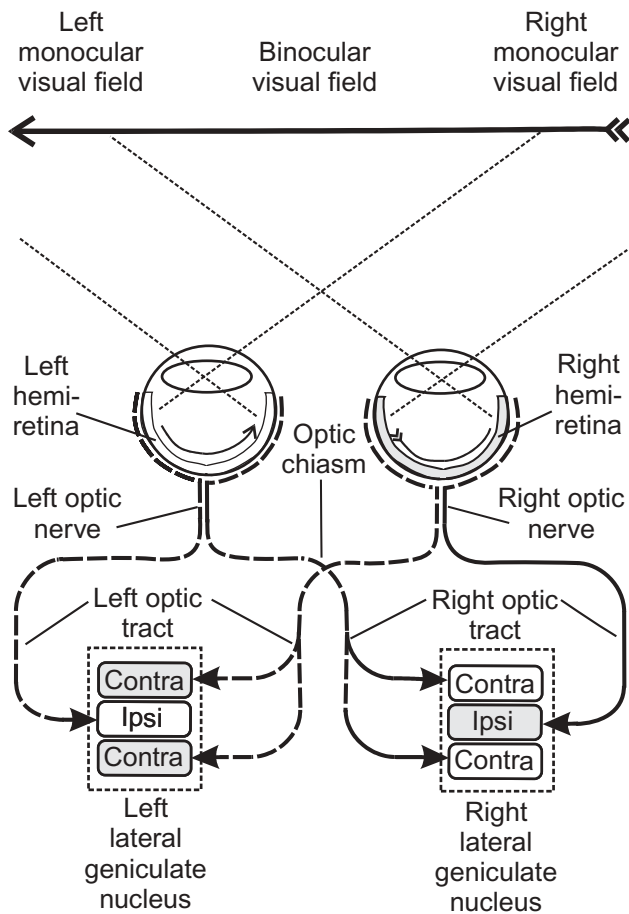


FIGURE 26-1. Drawing of ipsilateral and contralateral terminations of the optic tract in the dorsal lateral geniculate nucleus of a mammal. The shaded areas indicate the fields of termination from the right retina, and the unshaded areas indicate left eye terminations. In this hypothetical mammal, as in most nonprimates, contralateral terminations in the dorsal lateral geniculate are more numerous than ipsilateral terminations.

At the optic chiasm, the nerves partially decussate (cross the midline) and form the right and left optic tracts. The figure points out an important distinction between the optic nerve and the optic tract; i.e., the retinal axons contained in the left optic nerve all originate in the left retina, whereas those in the left optic tract originate from both the right and left retinas. In this example, each lateral geniculate consists of three termination zones—two from the contralateral eye and one from the ipsilateral eye. The shaded areas indicate the laminae where axons of the right optic nerve terminate.

An often overlooked feature of the dorsal lateral geniculate nucleus is the source of its predominant input. In cats, for example, the dorsal lateral geniculate nucleus receives most of its input from the striate cortex and other sources (visceral brainstem and intrinsic). About 30% of the synapses within the GLD are of cortical origin, whereas only 2–10% are from the retina. As we will discuss below, there are extensive reciprocal connections among visual cortical areas. This reciprocity of

information flow also extends to the level of the thalamus with the cortical input to the GLD.

Phylogeny of the Dorsal Lateral Geniculate Nucleus. The number of termination zones in the mammalian lateral geniculate can vary from three to six. In mammals with frontal vision, the termination zones form plates or **laminae**. Within this range, the patterning of ipsilateral and contralateral laminae can vary widely. Based on our understanding of mammalian evolution and lateral geniculate patterns, the most parsimonious assumption is that the dorsal lateral geniculate of the earliest placental mammals was similar to the pattern that is present in modern rodents and lagomorphs, as represented at the lower left in Figure 26-2, which is a cladogram of lateral geniculate organization in a selected group of placental mammals. This ancestral pattern persists in animals such as rodents and lagomorphs shown at the upper right. Such animals do not have well-developed spatial vision (visual acuity) and often rely on panoramic or near-panoramic vision as a defense against predation. In contrast, animals with good to excellent spatial vision, such as predatory carnivores or mammals that became adapted to life in the trees, have greater numbers of layers with varying proportions of ipsilateral and contralateral projections, with the contralateral projection being the larger. Old World monkeys, great apes, and humans have six layers that receive an equal distribution of ipsilateral and contralateral projections from the retina.

What is the phyletic relationship among the individual laminae of the dorsal lateral geniculate nucleus in different species of mammals? Is lamina A of a cat homologous to lamina 6 of a rhesus monkey or even to lamina A of a ferret (Fig. 26-3)? The answer to this question is “all and none.” The reason for this seemingly paradoxical answer is that we are dealing here with a **field homology** (see Chapter 1). Each component of the dorsal lateral geniculate nucleus of mammals is derived from the single dorsal lateral geniculate nucleus (as will be discussed below) of their early amniote ancestors, as is the dorsal lateral geniculate nucleus of reptiles and birds). When this unitary population of neurons became segregated into specialized ipsilateral and contralateral divisions, as in different species of mammals, or into separate subdivisions as we will see below in birds, these subdivisions retained their homologous relationship as a field to the ancestral condition. Thus, we cannot say that any single component of the dorsal lateral geniculate nucleus of one mammal is uniquely homologous to any other component in any other mammal; rather, all components of one species are homologous to all components of another as a set of derivatives of a single homologous developmental field.

Figure 26-3 shows the dorsal lateral geniculate nucleus of four frontal-eyed mammals that make extensive use of spatial vision: a tree shrew, a domestic cat, a ferret, and an Old World monkey. In such animals, the individual laminae typically receive exclusively ipsilateral or contralateral fibers. For example, in the tree shrew shown in Figure 26-3, the ipsilateral terminations (shaded in light gray) are in layers 1 and 5, and the contralateral terminations (shaded in dark gray) are in layers 2, 3, 4, and 6. In the rhesus monkey, the ipsilateral terminations are in layers 2, 3, and 5, and the contralateral terminations are in layers 1, 4, and 6. Similar patterns are seen in

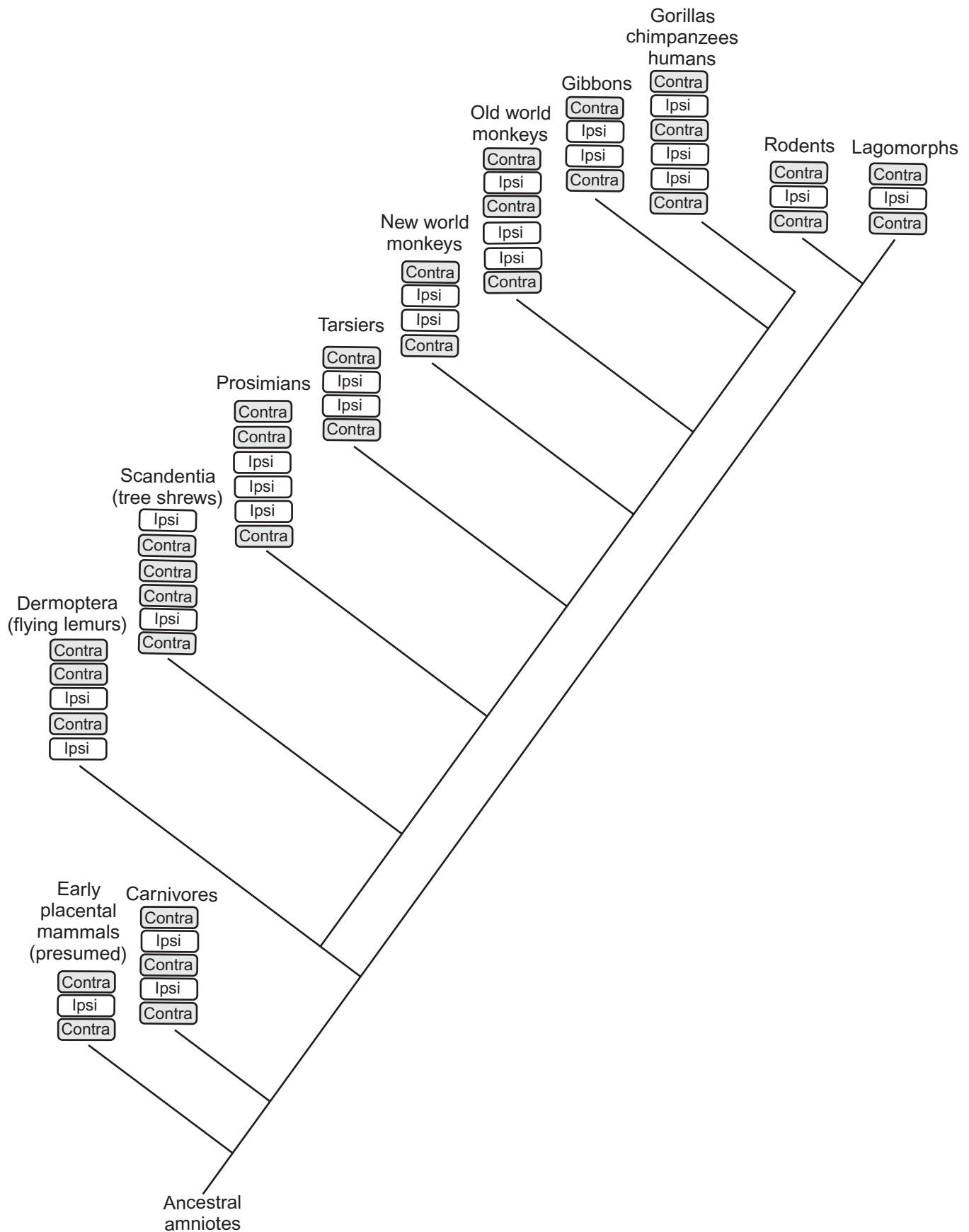


FIGURE 26-2. Cladogram showing the evolution of the dorsal lateral geniculate nucleus in certain mammalian taxa. Note the varying patterns of ipsilateral and contralateral retinal projections. The pattern in early placental mammals is shown at the lower left. In spite of their varying numbers of layers in the dorsal lateral geniculate, primates maintain equal distributions of projections from their ipsilateral and contralateral retinas. Adapted from Kaas (2004) and Sherman and Guillery (2004).

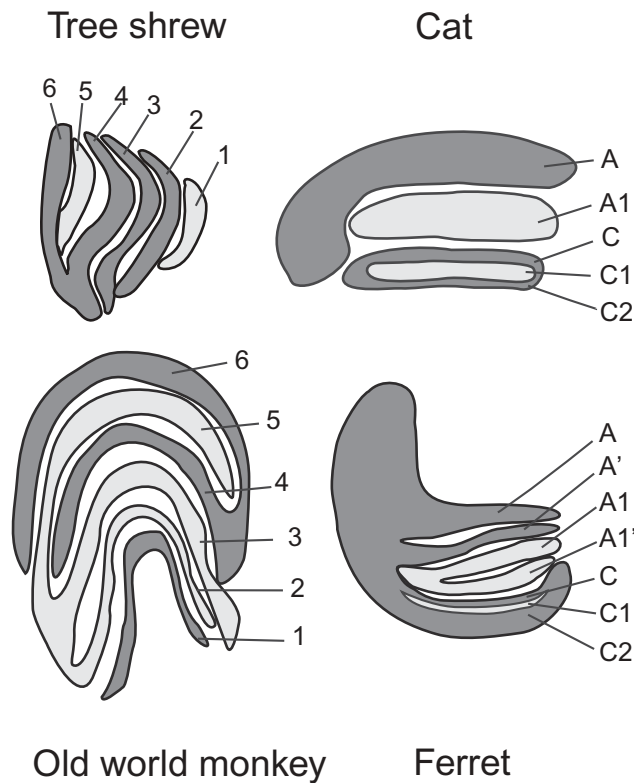


FIGURE 26-3. Drawings of various forms of the laminated pars dorsalis of the lateral geniculate nucleus on the left side in four species of mammals: a tree shrew, a cat, a rhesus monkey, and a ferret. The contralateral projections are shown in dark shading and the ipsilateral projections in light shading. Adapted from Casagrande and Norton (1991) and used with permission of Macmillan Press. In the tree shrew, note that the numbering of the layers is in the reverse order compared with that conventionally used in primates. If the numbers were to correspond, layer 1 in tree shrew would be layer 6, layer 2 would be 5, and so on.

cats, in which the ipsilateral terminal field is in laminae A1 and C1, and the contralateral projection is to laminae A, C, C2, and in ferrets in which the ipsilateral terminations are in laminae A1, A1', and C1, and the contralateral terminations are in laminae A, A', C, and C2.

Cell Types in the Dorsal Lateral Geniculate Nucleus. The two most thoroughly studied retinas are those of various primates and cats. The primate retina contains several classes of ganglion cells that send their axons to the dorsal lateral geniculate nucleus. These axons are named for the types of lateral geniculate cells upon which they terminate and have been designated by the letters M, P, and K for the types of target cells in the lateral geniculate upon which they terminate: **M** for the **magnocellular** ("large celled"), **P** for the **parvocellular** ("small celled," also spelled parvicellular), and **K** for the **koniocellular** ("dust celled," meaning very small celled). Within the lateral geniculate, these target cells are arranged into laminae. Figure 26-4 presents a schematic representation of the lateral geniculate nucleus of an Old World monkey and cat. The

laminae that receive the axons from the ipsilateral and contralateral eyes are indicated within each animal's lateral geniculate.

The physiological characteristics of the M, P, and K cells of the retinas of monkeys correspond roughly to cell types that have been reported in cat retinas, which are referred to only by the letters X, Y, and W. The latter inputs are shown in the cat lateral geniculate in Figure 26-4. The table in the figure indicates the correspondences between the retinal ganglion cells of cats and monkeys.

In monkeys, the magnocellular component comprises two layers—layers 1 and 2. Layer 2 receives axons from the ipsilateral eye and layer 1 from the contralateral eye. Laminae 3–6 are parvocellular. Diurnal primates have a greater proportion of the parvocellular part of the dorsal lateral geniculate nucleus than do nocturnal primates, especially in the areas of this nucleus that are devoted to the central part of the visual field, where acuity is highest. The koniocellular components of the monkey dorsal lateral geniculate nucleus are found in the spaces between the laminae. In cats, the X and Y retinal inputs are not completely differentiated into separate layers. Lamina A (from the contralateral eye) and lamina A1 (from the ipsilateral eye) both share X and Y inputs, whereas lamina C (from the contralateral eye) receives a Y input only. The W input is into laminae C1 and C2, which are from the ipsilateral eye and contralateral eye, respectively.

Each of these retinal ganglion cell types is associated with different physiological characteristics. These characteristics are considered to be functional "channels" that bring different aspects of the visual world to the visual areas of the forebrain. These channels are independent parallel pathways to the visual cortex. Table 26-1 summarizes the functional differences between the three retinal ganglion cell classes. The P pathway or channel leaves the retina via the axons of the midsize ganglion cells and terminates in the parvocellular laminae of the dorsal lateral geniculate nucleus. These ganglion cells are mainly found in the foveal region of the retina, which is the region of highest visual acuity (sharpest vision). In monkeys, the M pathway is associated with large retinal ganglion cells known as parasol cells for their umbrella-shaped dendritic trees and terminates on the magnocellular laminae of the dorsal lateral geniculate nucleus. The M ganglion cells are typically found in the periphery and are quite responsive to stimuli that move. The K pathway terminates on the koniocellular components of the dorsal lateral geniculate nucleus. These ganglion cells are the most variable in their properties and indeed may actually consist of several different cell types, at least one type of which is known as bistratified.

These three channels differ in the sizes of their receptive fields, their ability to resolve small differences between stimuli, their responsiveness to temporal changes in stimuli and contrast changes, as well as other properties. Cells with P-, M-, and K-like properties—the X, Y, and W cells—have been described in nonprimate mammals, such as cats, ferrets, rats, tree shrews, opossums, and rabbits. Although widely distributed throughout mammals, the P/X, M/Y, and K/W channels have not been widely reported in nonmammals. Whether this lack is due to the uniqueness of these neuronal systems in mammals or to the paucity of electrophysiological studies in nonmammalian preparations is not clear at present. Certain characteristics

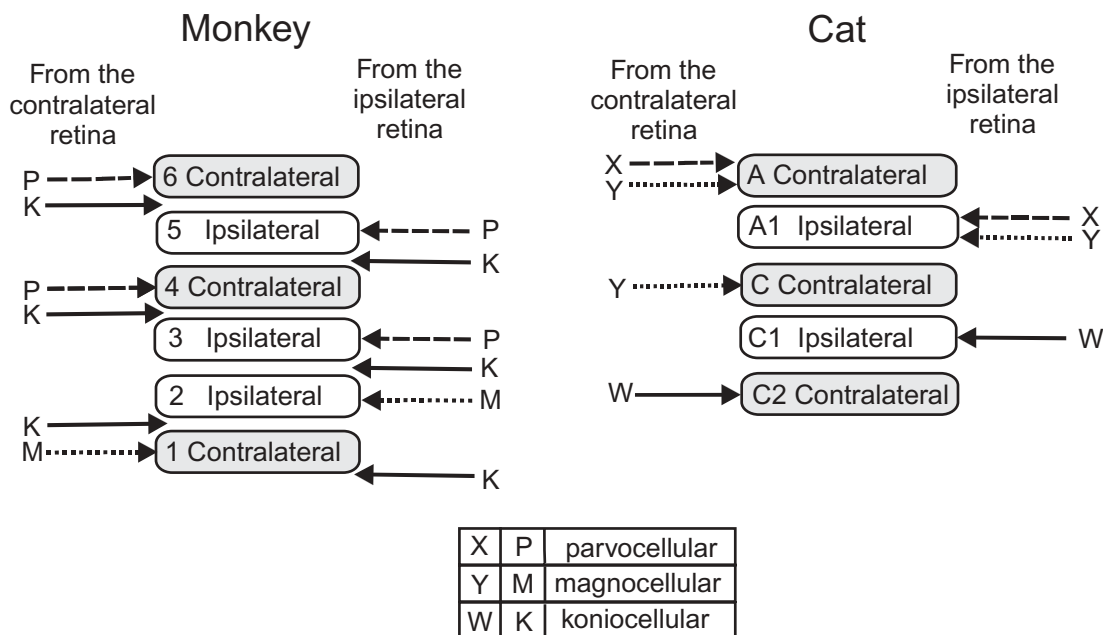


FIGURE 26-4. The patterns of termination of the parvocellular (P), magnocellular (M), and koniocellular (K) pathways from the retina in the dorsal lateral geniculate nucleus of a monkey and the corresponding patterns of X, Y, and W terminations in a cat. Adapted from Sherman and Guillery (2004).

TABLE 26-1. Classes of Cells in the Visual Lemnotheralamus of Primates					
Primate Cell Class	Non-primate cell class	Retinal Ganglion Cell Type	Lateral Geniculate Cell Type	Layer of Termination in Striate Cortex	Some Physiological Properties
P	X	Midget ganglion cells (mostly in fovea)	Parvocellular	4C β	Small receptive field
					High spatial resolution, color
					Low temporal resolution
					Low sensitivity to contrast and motion
M	Y	Parasol cells (mostly in periphery)	Magnocellular	4C α	Medium receptive field
					Moderate spatial resolution
					High temporal resolution
					High sensitivity to contrast and motion
K	W	Bistratified cells, among others (variable location)	Koniocellular	2 and 3	Medium receptive field
					Moderate spatial resolution
					Variable sensitivity to movement

of P/X and M/Y cells have been reported in nonmammals, especially in birds, which have independently evolved visual systems that are the equal of (and in some instances superior to) the best visual systems of mammals, including the primates. For the present, however, the P/X, M/Y, and K/W channels that have been fully characterized in mammals by morphological, chemical, and electrophysiological criteria are not known in nonmammalian vertebrates.

Figure 26-5 represents the pathway from the retina to the lateral geniculate nucleus to the visual cortex of the M, P, and

K pathways in a primate. For simplicity, not all of the laminae of the lateral geniculate are shown. From the retina, these three pathways make their way to their respective laminae in the dorsal lateral geniculate, the parvocellular laminae for the P pathway, the magnocellular laminae for the M pathway, and the spaces between the laminae for the K pathway. The K pathway is relayed to layers 2 and 3 of the visual cortex. The axons leaving the magnocellular and parvocellular laminae of the lateral geniculate ascend to a subdivision of layer 4, called layer 4C. Layer 4 has been further subdivided into 4C α and 4C β . The

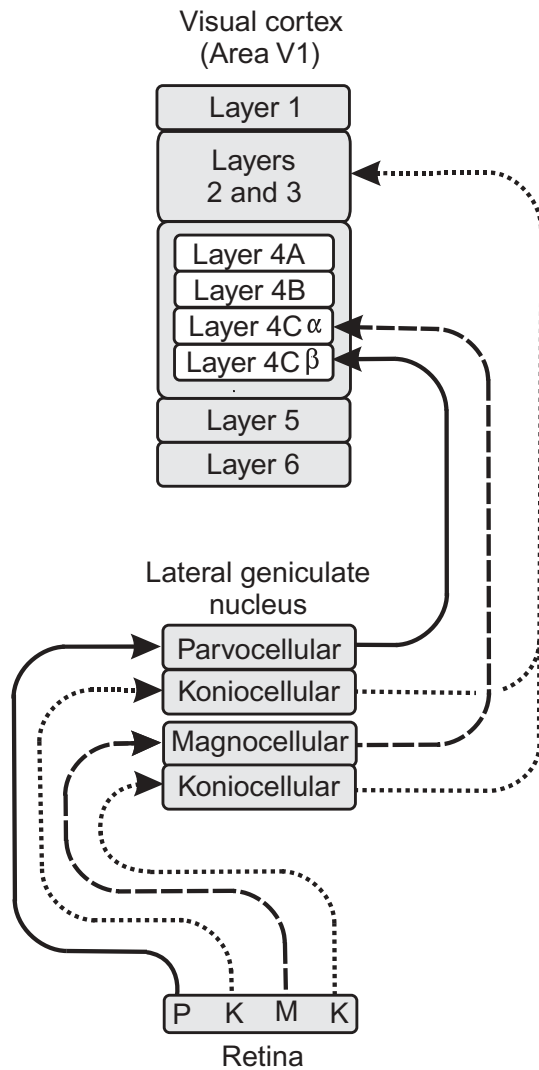


FIGURE 26-5. The P, M, and K pathways from the retina through the dorsal lateral geniculate to their target layers in the striate visual cortex of a primate. Not all laminae of the dorsal lateral geniculate are shown.

M pathway terminates in layer 4C α , and the P pathway ends in layer 4C β . We will follow these pathways further through the cortex later in this chapter.

Ventral Division of the Lateral Geniculate Nucleus. A **ventral division** of the lateral geniculate nucleus is also present in the thalamus of mammals, but it is considered to be a part of the ventral thalamus (see Chapter 19). This structure, which is a typical feature of vertebrate visual systems, receives axons from the retina but does not send its efferents to the telencephalon as do the lemnothalamic and collothalamic visual nuclei of the dorsal thalamus. In primates, the ventral part of the lateral geniculate nucleus is known as the **pre-geniculate nucleus**, and it is very variable in its size and location. For example, in prosimians it is located on the lateral surface of the dorsal lateral geniculate, whereas in anthropoids, it has shifted so far dorsally that one author has described it as an “eyebrow” over the dorsal division.

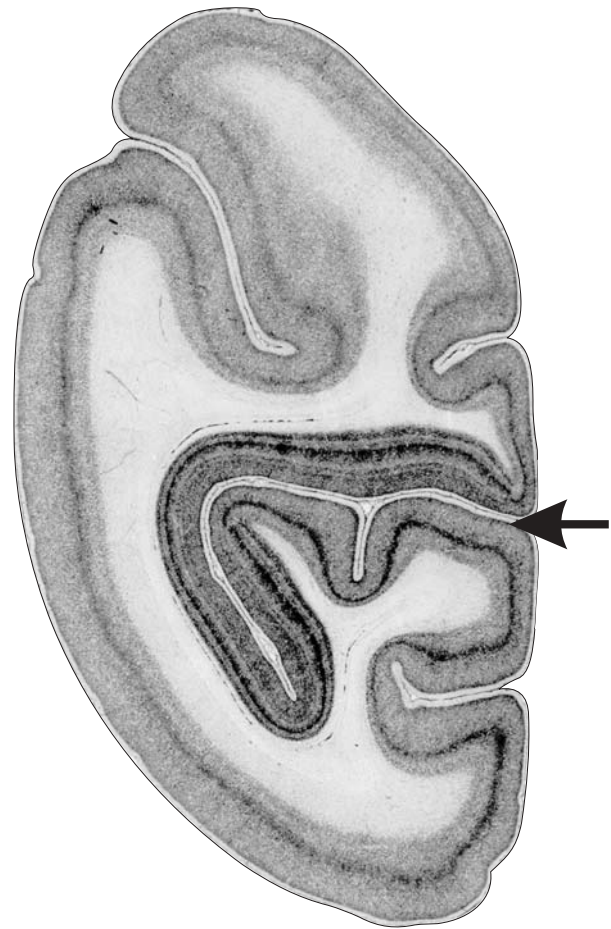


FIGURE 26-6. Photomicrograph of a section through the striate cortex—in the involuted area internal to the arrowhead—in a mammal (*Procyon lotor*). Note the particularly dark stripe in this region that marks layer IV. Photomicrograph courtesy of Wally Welker.

Striate and Extrastriate Visual Cortices. The lemnothalamic visual efferents from the dorsal lateral geniculate nucleus terminate in the most posterior region of the cerebral hemisphere, in part of the **occipital lobe**. This area of neocortex is known as the **striate cortex** because of the prominent stripe or band located within layer 4. This stripe is called various names after the scientists who described it, such as the **stripe (or line) of Gennari**, after the eighteenth-century Italian physician Francesco Gennari. It also is known as the **outer stripe of Baillargier**, after the nineteenth-century French physician Jules Baillargier, who observed this band and one other while he was describing the lamination of the cerebral cortex. This stripe is formed by the heavily myelinated axons of dorsal lateral geniculate neurons as they pass through layer 4 en route to their destinations within this region of cortex. Figure 26-6 shows a low-power photomicrograph of striate cortex with a prominent stripe in a raccoon. Figure 26-7 shows the location of the striate cortex in six mammals: a marsupial (opossum), a rodent (rat), a lagomorph (rabbit), an arboreal eulipotyphlon [tree shrew, formerly classified as an insectivore (see Chapter 4)], and a prosimian primate (a bushbaby).

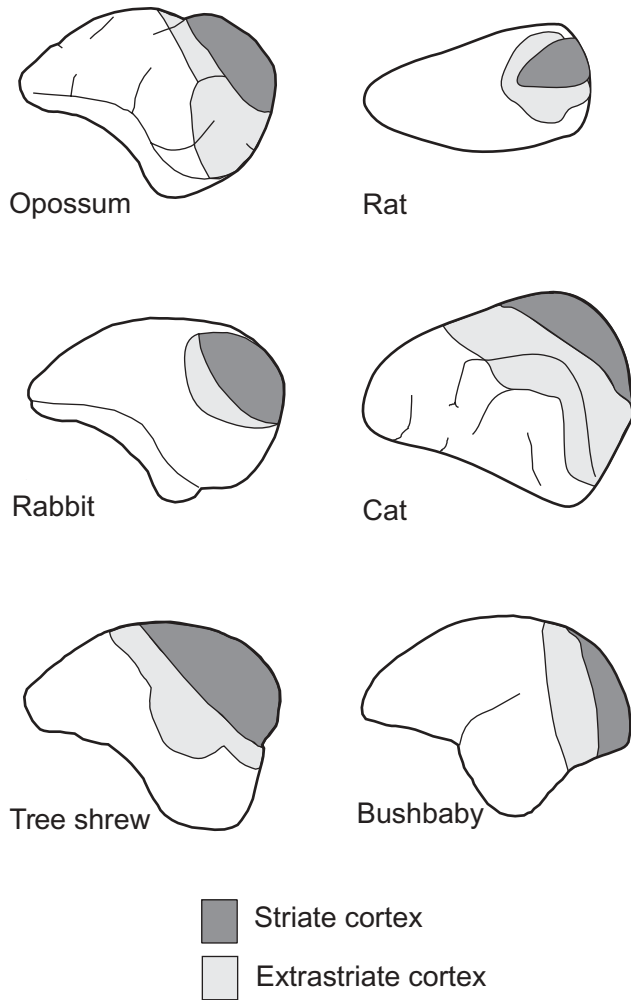


FIGURE 26-7. Variations in the extent of striate and extrastriate visual cortex in six mammals. In each drawing, rostral is toward the left.

In the nomenclature of the German neurologist Korbinian Brodmann (1868–1918), the striate cortex is **area 17**, which corresponds to area **V1**. The visual collothamic termination area in the extrastriate cortex is in **area 18** and **area 19**, which are comparable to areas **V2** and **V3**, and in a number of additional visual areas in the occipitotemporal cortical region. Why have two different systems for naming visual areas? The Brodmann areas were determined according to anatomical criteria, whereas the areas **V1–V4** were identified according to physiological criteria. Some vision scientists prefer yet a third system, one proposed by Constantin von Economo (1876–1931), that uses letters of the alphabet to identify various cortical regions. With regard to the numbering of the cortical layers, both Roman numerals and their corresponding Arabic numerals have been used by different scientists. The current practice in the numbering of the layers in the visual cortex seems to favor the Arabic numerals and so we will use those in this chapter. As more recent work has been done mapping the various visual cortical areas in a variety of mammals, additional terms have been added to the lexicon, such as the middle visual temporal

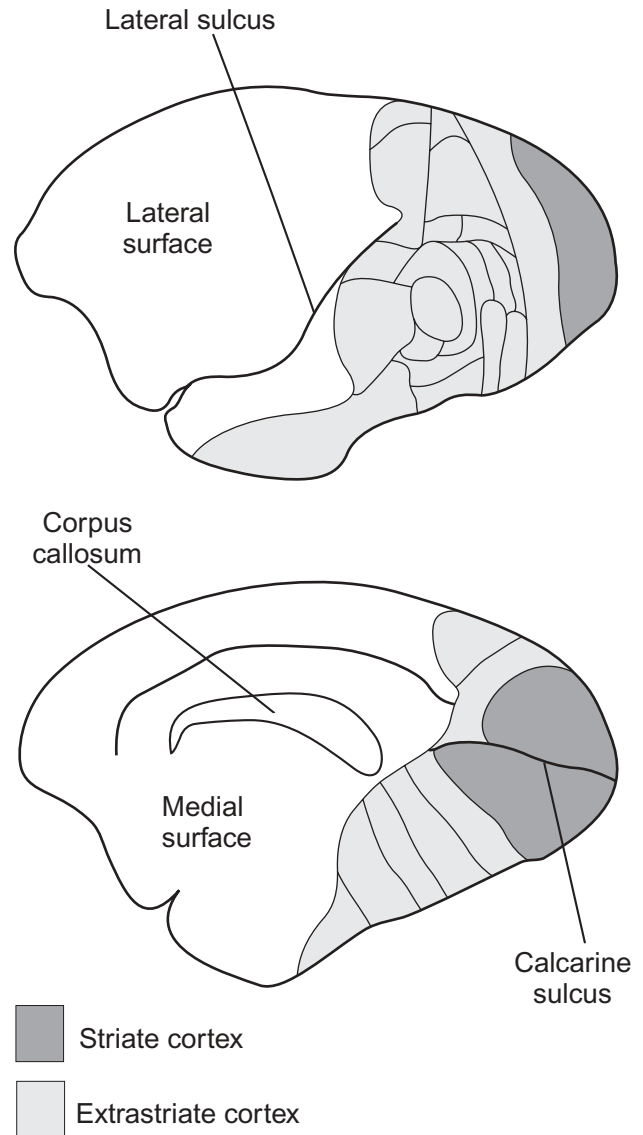


FIGURE 26-8. Drawing of the striate and extrastriate visual cortices of an owl monkey. The subdivisions within the extrastriate visual cortex indicate multiple representations of the visual world. Based on data from Allman and McGuinness (1988) and Sereno and Allman (1991).

area (MT), dorsomedial area (DM), and dorsolateral area (DL) of primates. DL is about the same as the area referred to as **V4**, depending on the particular study, and MT is generally regarded as being equal to **V5**.

Most maps of striate cortex show its location on the lateral surface of the brain, which in many instances gives a misleading underestimate of the total area, because this cortical region continues onto the medial surface. Figure 26-8 shows the striate cortex of an owl monkey on both the lateral and medial surfaces. Note on the medial surface the presence of a deep sulcus, the **calcarine** (claw-like) **sulcus**, which is a prominent feature of the telencephalon in primates. A considerable amount of striate cortex is “buried” within the depths of this

sulcus. Buried striate cortex (as well as buried cortex with other specializations) occurs commonly in gyrencephalic mammals.

The efferents of the striate cortex are predominantly to extrastriate cortex, but striate cortex also projects to sites in the diencephalon and mesencephalon, including the dorsal lateral geniculate nucleus, superior colliculus, and other targets of the optic tract. The high degree of dependence of many (and perhaps most) diurnal species of mammals on vision can be seen in the large proportion of cortex devoted to vision. Some of the cortical areas that respond to visual stimulation overlap areas traditionally regarded as somatosensory or motor. Typically, the total area of neocortex devoted to both striate and extrastriate cortices is 45–50%, but when diurnal mammals are compared with nocturnal mammals, the percentages are higher for the diurnal by 10–15%. In diurnal Old World monkeys, the total area of cortex responsive to visual stimuli to at least some degree is now estimated to be approximately 75% and may be even higher in great apes and humans.

Retinotopic Organization. An important characteristic of the central visual system is its retinotopic organization, which is a form of topographic organization found in sensory and motor systems (see Chapter 2). In a retinotopic organization, the relationship between each point on the retinal surface, which corresponds to a point in visual space, is preserved in the subsequent cell populations of the visual pathway, for example, from the dorsal lateral geniculate nucleus to the striate cortex. Although the topology and topography are preserved, the proportional representations of each area are not generally maintained. Thus, the central retina, which in mammals is the area of highest visual acuity, is represented by a greater proportion of neural tissue in the striate cortex than it is on the retina. This increase is known as the **magnification factor**. Although the area of representation is increased in this manner, it should be noted that the amount of cortex allotted to a given number of receptor cells remains the same across the cortical surface. The greater density of receptor cells (cones) in the central retina is directly proportional to the greater area of cortex that receives visual input from it.

The striate visual cortex has a highly retinotopic organization. In the extrastriate cortex, the situation is considerably more complicated because not one but a multiplicity of retinotopic organizations is present. The subdivisions of the extrastriate visual cortex in an owl monkey, which is a New World monkey, are shown in Figure 26-8 and consist of 24 separate regions in which retinotopic maps can be found. For the sake of simplicity, we have not provided the names of the individual regions. In Old World monkeys, 36 regions have been found. Prosimian primates, as well as carnivores, rodents, and lagomorphs, have at least 13 or 14 extrastriate visual areas.

The maps within various parts of extrastriate cortex differ from one another in a number of respects; for example, adjacent maps may be mirror images of one another or they may only map part of the visual field rather than the whole field. Indeed, a number of these visual areas overlap areas of cortex traditionally considered to be motor or somatosensory, as mentioned above. Some of these areas seem to be more involved with color; others more with the shape of objects, and still others more with stimuli that move.

Figure 26-9 shows an example of retinotopic organization in the **middle temporal area** or **area MT** of the **extrastriate cortex** of an owl monkey. The extrastriate cortex is the collicular cortex, which we will discuss below; we turn to it here simply for illustrating retinotopic organization. The upper diagram in Figure 26-9 represents location in visual space. The plus numbers represent the degrees of elevation of the target in the upper visual field; the minus numbers represent the degrees of elevation of the target in the lower visual field. The lower diagram indicates the positions of these visual field locations within area MT. The extrastriate visual cortical areas contain a large number of such retinotopically organized areas. Each of the subregions within striate and extrastriate visual cortex contains a complete or partial retinotopic map.

Columnar Organization. In the 1960s, David Hubel and Torsten Wiesel documented the existence of a vertical (i.e., columnar) organization of cat visual cortex; that is, the visual cortex is organized in a series of vertical columns, with each column conveying information about a variety of stimulus properties such as direction, orientation, and color. Moreover, each eye has its own set of columns in the cortex; that is, the

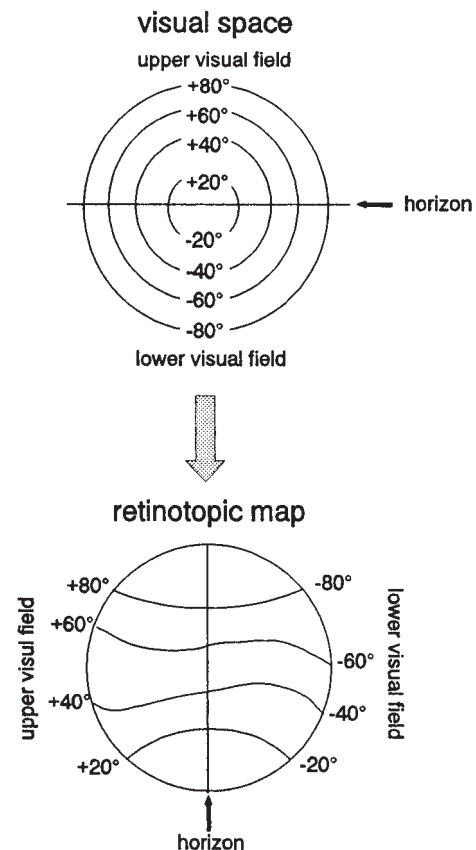


FIGURE 26-9. Diagram of retinotopic organization in extrastriate area MT (middle temporal area) in an owl monkey. The positive numbers in the top figure indicate degrees of elevation into the upper visual field. The negative numbers indicate degrees of elevation into the lower visual field. The bottom figure shows how points in space are represented in area MT.

segregation into ipsilateral and contralateral subdivisions persists at the cortical level in a covert form. Thus, if an eye is removed surgically, the physiologist finds that certain columns are active while neighboring columns are "silent." Since a given eye is said to dominate a particular column, this distribution of right and left eye inputs to the right or left visual cortex is known as **ocular dominance columns**. These covert columns can be visualized by a variety of histochemical techniques. One method involves the mitochondrial enzyme, cytochrome oxidase, which increases in concentration when cells are metabolically active, such as when they are being stimulated. Staining for cytochrome oxidase in the cortex of an animal that has had one eye open and one eye closed reveals a series of perpendicular bands of staining within striate cortex that are particularly dark in layer 4, the granule cell layer that receives its predominant input from the dorsal lateral geniculate nucleus. Other techniques reveal the existence of these bands in other layers. Indeed, many anatomists and physiologists believe that the columns are continuous throughout the full depth of the cortex.

Figure 26-10 illustrates ocular dominance columns in a small region of striate cortex on the right side. The shaded regions receive input from the contralateral (left) eye, and the unshaded regions receive input from the ipsilateral (right) eye. Notice that the ocular dominance zones extend throughout the entire thickness of the cortex (layers 1–6). The ocular dominance zones are further subdivided into functionally different, smaller columns, called **orientation columns**, in which the cells in one such column may prefer vertical lines, while some of its neighboring columns may prefer varying degrees of diagonal lines, and still other columns would selectively respond to horizontal lines.

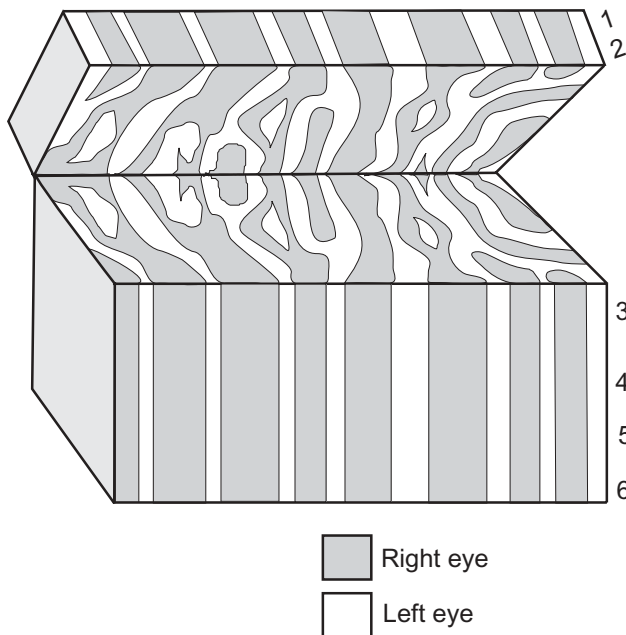


FIGURE 26-10. Diagram of ocular dominance columns in a small region of the striate cortex of a mammal. A slab of tissue has been removed at the top to reveal the three-dimensional structure of the columns. The numerals indicate the layers of the cortex.

Within the ocular dominance columns revealed by cytochrome oxidase staining, the staining is not uniform; instead, it is patchy with lighter and darker regions, especially within layers 2–3. The darker regions (with more intense activity) have been described as **blobs**, **puffs**, or **patches** by various workers. These differences in staining density represent differences in functional organization. The cells found within the darker regions, called **blob cells**, differ from the cells found in the lighter regions, **interblob cells**, in several characteristics. A greater proportion of the blob cells respond differently to colors but do not respond very well to differences in the orientation of the stimulus (horizontal, vertical, or diagonal). The interblob cells tend to respond to stimulation of either eye, whereas blob cells are more monocular and also more responsive to the overall shape of an object rather than to its fine details. Cytochrome oxidase histochemistry of area V2 has revealed a corresponding pattern of alternating thick and thin cytochrome oxidase-rich **stripes** separated by **interstripes** that show low cytochrome oxidase activity.

Figure 26-11 shows a schematic representation of a pair of adjacent ocular dominance zones in the striate cortex. One zone is dominated by the ipsilateral eye and the other by the contralateral eye. Within each ocular dominance column is a series of orientation columns, each of which prefers a different stimulus orientation. Within the orientation columns in layers 2–3 are the blobs. Pairs of adjacent ocular dominance columns—with their integral orientation columns, blobs, and interblobs—are known as **hypercolumns** and appear to be a kind of basic organizational unit for analyzing the composition of a particular region of visual space.

Below these cortical representations in Figure 26-11 is a pair of lateral geniculate nuclei in a reduced form. The geniculostriate pathways from the M(Y), P(X), and K(W) laminae of the lateral geniculate are shown. The K pathway ascends to the blobs within layers 2 and 3. The P pathway terminates in cortical layer 4C β . Axons of the 4C β neurons terminate in both the blob and interblob regions of layers 2 and 3. The M pathway axons end on the cells of layer 4C α , the axons of which terminate in the adjacent layer 4B.

Clear instances of ocular dominance columns have been reported in a variety of Old World monkeys and apes and in carnivores. The columns are less clear in prosimians and New World monkeys and appear to be absent in rodents and lagomorphs. This distribution across species suggests that the presence of ocular dominance columns may be related to the process of stereoscopic vision.

Visual Streams. Figure 26-12 displays the visual cortical regions of a monkey. The visual areas of the occipital lobe have been unfolded out so as to show both the medial and lateral surfaces of the cortical sheet. Area V1 is the striate cortex. Areas V2, V3, and V4 each contain retinotopic maps of various portions of the visual field. Areas V2, V3, and V4 receive little or no input from the dorsal lateral geniculate but instead receive their afferents from V1. Area MT contains a large representation of the entire contralateral visual field with an emphasis on central vision. Its neurons are particularly responsive to retinal disparity, which is the slight difference in the images of the two eyes that results in stereoscopic vision as well as motion, including complex motion.

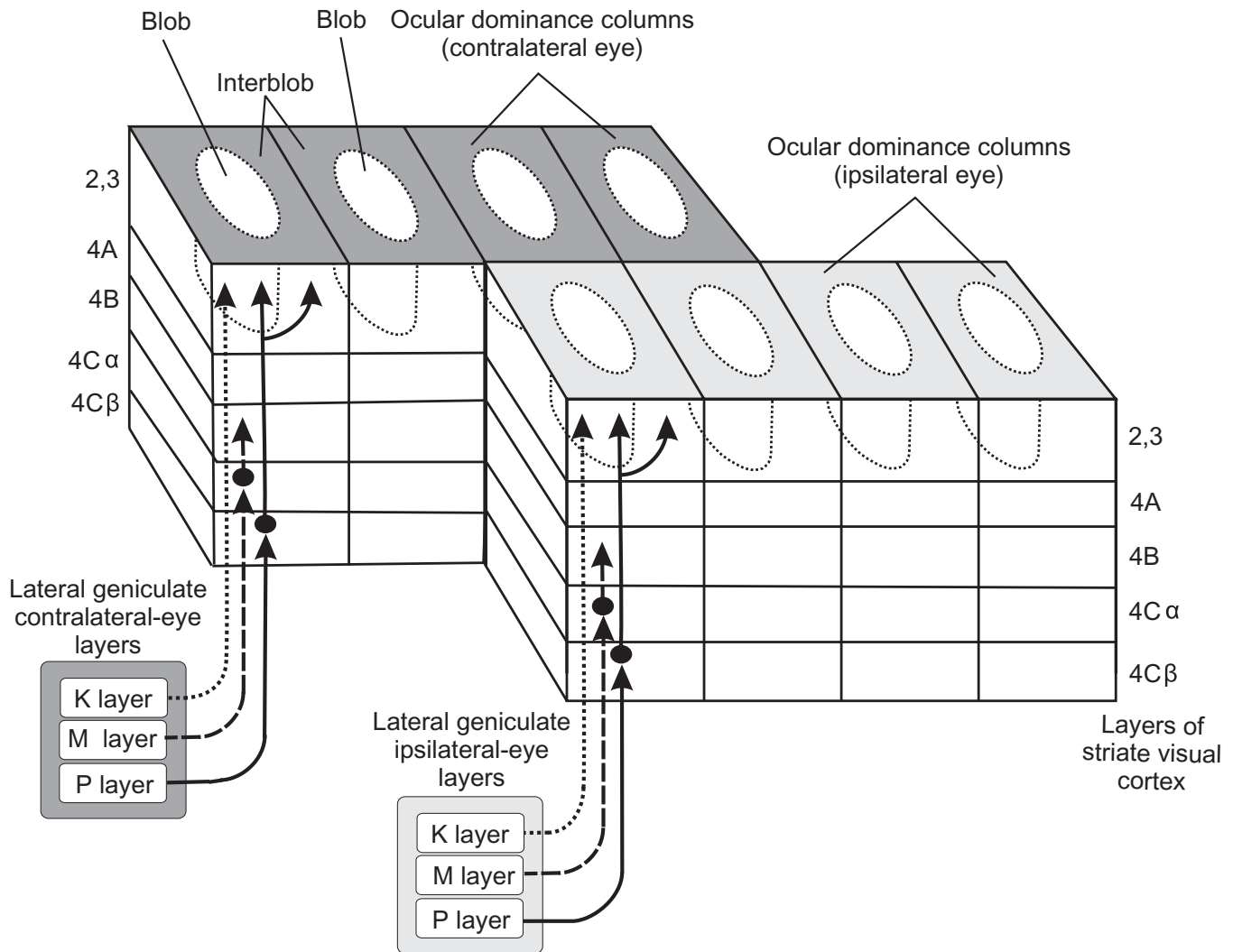


FIGURE 26-11. Diagram of a hypercolumn formed by a pair of adjacent ocular dominance columns. Within each ocular dominance column can be seen other forms of columnar organization such as blob and interblob columns.

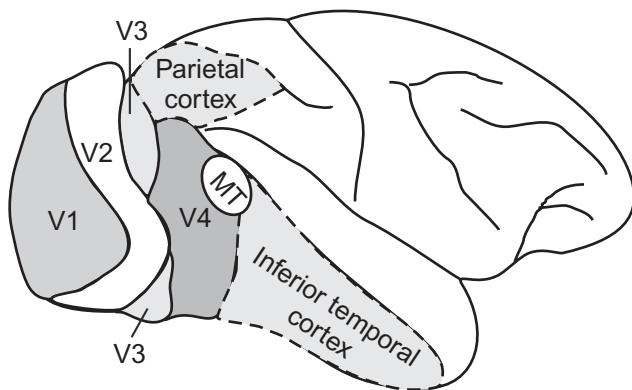


FIGURE 26-12. Visual cortical regions of a monkey (see Fig. 26-8 for more detail). The cortex of the occipital lobe has been unfolded outward to show both the medial and the lateral surfaces of the cortical sheet. Area V1 is the striate cortex. Adapted from Ungerleider and Pasternak (2004) and used with permission of MIT Press.

The striate visual cortex is the origin of a bifurcated cascade of pathways to other visual cortical areas as well as a number of cortical regions that are not traditionally considered as visual cortex. The two visual streams emerge as a cascade from V1, V2, and V4 as shown in Figure 26-13. The ventral stream proceeds to V4 and inferior temporal cortex; the dorsal stream progresses to area MT and the parietal cortex. Both streams are then relayed to the prefrontal cortex of the frontal lobe. Figure 26-14 shows more details about the interconnections within the two streams. Many of the connections shown in this figure are bidirectional.

These two visual streams differ in their physiological and behavioral functions. The ventral stream seems to be involved in the processing of color and form information. It is sometimes referred to as the *what is it?* pathway. The dorsal stream seems to be more concerned with motion and location in space and has been termed the *where is it?* pathway. These functional designations are convenient oversimplifications that gloss over the many subtleties and complexities of these two functional

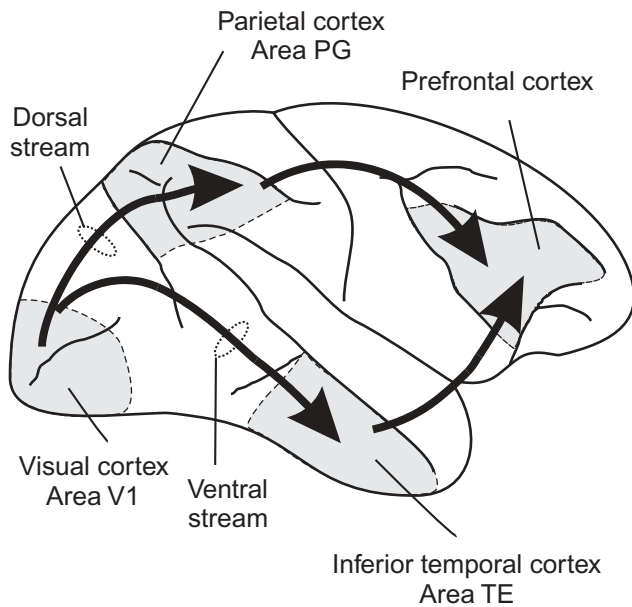


FIGURE 26-13. The dorsal and ventral cortical visual streams. These divergent streams emerge from visual cortical area V1 and eventually are relayed to the prefrontal cortex. Adapted from Ungerleider and Pasternak (2004) and used with permission of MIT Press.

streams. Moreover, the literature on this topic is beginning to suggest that the dorsal and ventral streams may be further subdivided into additional functionally distinct streams.

Collothalamic Visual Forebrain

As we have already seen, the main source of input to the striate cortex from the retina is via the dorsal lateral geniculate nucleus. The principal source of afferents to the extrastriate visual cortex is via the collothalamic visual pathway from the retina to the superior colliculus to the lateralis posterior/pulvinar complex and hence to the cortex (see Fig. 26-15). The collothalamic visual nucleus in mammals is called **nucleus lateralis posterior** or, in primates, the **pulvinar**, which derives from the Latin word for a pillow or cushion. Primates also have a nucleus called lateralis posterior, but it is not a collothalamic visual nucleus. In cats, on the other hand, both nucleus lateralis posterior and the pulvinar are collothalamic visual nuclei. The pulvinar in both cats and primates consists of a number of subdivisions of which some, but not all, are collothalamic visual nuclei.

The primate pulvinar consists of several subdivisions of which the **inferior pulvinar** is the target of the projections from the superior colliculus. The inferior pulvinar itself may be further subdivided into entities that themselves differ on the basis of cell types and organization as well as histochemistry. The medial inferior pulvinar sends a dense projection to the MT region of extrastriate visual cortex. Other inferior pulvinar subdivisions include a central zone, a lateral zone, and a lateral-shell zone. All four subdivisions of the inferior pulvinar receive retinotopically organized projections from V1. A fifth division, the posterior zone, also has been reported, but it might actu-

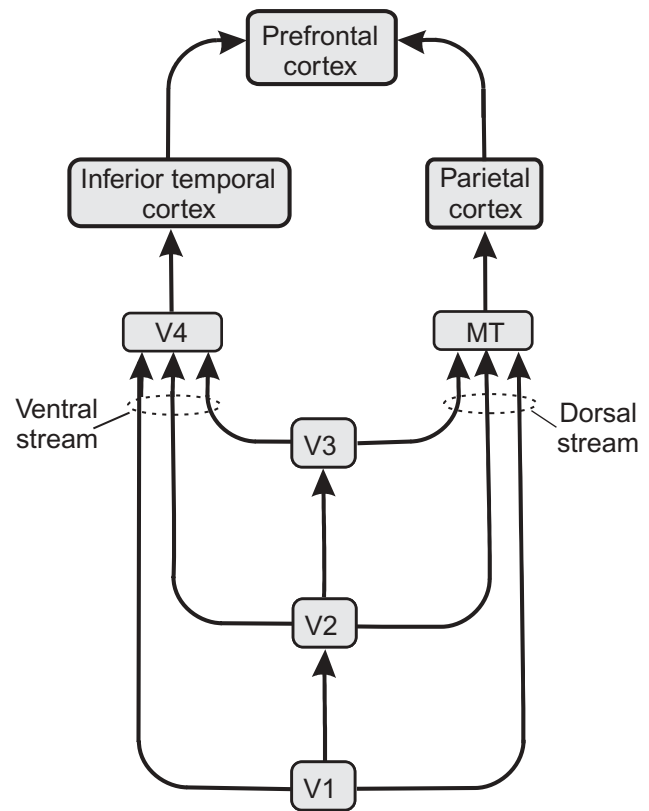


FIGURE 26-14. A simplified schematic representation of the cortical connections that comprise the dorsal and ventral cortical visual streams. Many of the connections shown are bidirectional.

ally be an extension of the central zone, since these two regions are contiguous and have similar histochemistry. All of the subdivisions of the inferior pulvinar have connections, apparently reciprocal, with regions of extrastriate visual cortex.

Collothalamic Inputs to Visual Pallium. The relationship between the lateralis posterior/pulvinar complex and the extrastriate cortex is intricate and involves reciprocal connections between this collothalamic cell group and both extrastriate and striate cortices. Moreover, the nucleus appears to be divided into striate-recipient and extrastriate-recipient zones in addition to the zone that receives axons from the superior colliculus. Like the extrastriate cortex that it innervates, the lateralis posterior/pulvinar complex contains multiple representations of the visual field with retinotopic organization. Again, like the extrastriate visual cortex, the retinotopic organization is not as precise as is found in the dorsal lateral geniculate nucleus and striate cortex.

A secondary source of afferents to the extrastriate visual cortex is the dorsal lateral geniculate nucleus, as shown in Figure 26-15, although this projection is considerably more modest than the projection of the dorsal lateral geniculate nucleus to striate cortex. Likewise, the lateralis posterior/pulvinar complex gives rise to a minor projection to the striate cortex.

In addition to projecting to extrastriate cortex, the lateralis posterior/pulvinar complex gives rise to a minor collateral

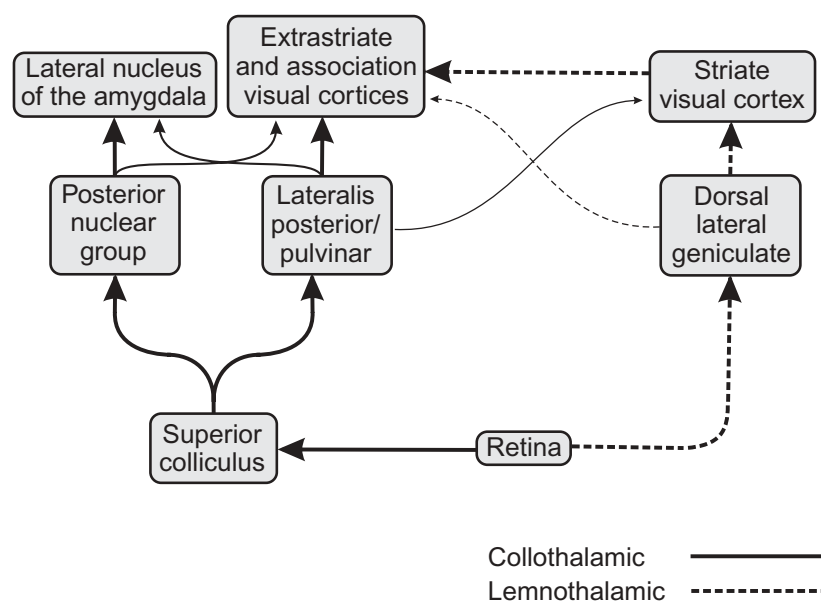


FIGURE 26-15. Summary of collothamic and lemnothalamic visual pathways in mammals. Heavy lines indicate major projections. Thin lines indicate minor projections.

projection to the lateral nucleus of the amygdala. As discussed in Chapter 25, the lateral amygdaloid nucleus is a component of the frontotemporal amygdala. While the lateral nucleus is reciprocally connected with the hippocampus, it also receives direct collothamic projections and is highly interconnected with frontal and temporal association cortices. The lateral amygdala also receives collothamic visual inputs from components of the posterior nuclear group, such as the supra-geniculate nucleus, which also gives rise to a minor projection to retroinsular, temporal association cortex. Thus, while some extrastriate association cortices receive a major input from LP/pulvinar and a minor input from the posterior nuclear group, the lateral amygdala has the reciprocal pattern of circuitry—a minor input from LP/pulvinar and a major input from the posterior nuclear group (Fig. 26-15).

Visual System Processing. To return to our fox in the meadow who was processing the retinal image of the ground squirrel, the fox located the squirrel with his earlier stages of processing, that is, his superior colliculus, which has a precise retinotopic organization. He interpreted the retinal images with the lemnothalamic, collothamic, intercortical, and intra-cortical pathways of a number of his multiple visual cortical areas. Other areas of extrastriate cortex, along with multimodal association cortices, limbic cortices involved in memory functions (as will be discussed in Chapter 30), and the lateral amygdala and its circuitry allowed the fox to process whether encounters with similar stimuli in the past were satisfactory or not so that he could come to a decision as to whether or not to pounce. Exactly how and where the information that is processed in these multiple cortical regions comes together to form perceptions of whole objects, with the qualities of form, color, position, and motion all integrated, and how the cortical regions organize unfamiliar patterns of stimuli into meaningful visual images are the subjects of intensive investigation by vision scientists.

PATHWAYS TO THE VISUAL TELENCEPHALON IN REPTILES AND BIRDS

The collothamic and lemnothalamic visual pathways that were described for mammals above and in Chapters 22 and 25 also occur in reptiles and birds. The emergence of substantial information about the visual systems of nonmammals, however, poses a number of nomenclatural problems for students of visual system comparative anatomy and evolution. These difficulties stem from the fact that many of the neuronal groups in the thalamus already had already been assigned names before their affiliation with the visual system was understood, particularly for the lemnothalamic and ventral thalamic visual nuclei. This led to a variety of different names for structures in different species even though these structures each have the same relationship to the retinal, diencephalic, and telencephalic components of the visual pathway. The task of the student would be simplified if the neuronal population in the dorsal thalamus that receives axons directly from the retina and in turn sends its axons directly to the visual pallium had the same name in all vertebrates; regrettably this is not the case. Table 26-2 lists the comparable collothamic and lemnothalamic visual nuclei in the three groups of amniotes. In this table, we have used the term *dorsal lateral geniculate nucleus* for the lemnothalamic target of the optic tract, since there seems to be universal agreement that this is the equivalent cell group to the structure of the same name in mammals.

Figure 26-16 summarizes both the collothamic and lemnothalamic visual pathways from the thalamus to the telencephalon. Note that mammals have two collothamic visual pathways to the pallium—one from LP/pulvinar predominantly to extrastriate visual cortices and another from the posterior nuclear group predominantly to the lateral nucleus of the amygdala.

TABLE 26-2. Thalamic Sources of Afferents to the Visual Telencephalon of Amniotes		
	Lemnothalamic	Collothalamic
Mammals	Dorsal lateral geniculate nucleus (various numbers of laminae)	N. lateralis posterior and/or pulvinar Posterior nuclear group (see Chapter 22)
Reptiles	Dorsal lateral geniculate nucleus (see Chapter 22)	Nucleus rotundus
Birds	Dorsal lateral geniculate nucleus (nucleus opticus principalis thalami or OPT complex), which includes: Nucleus dorsolateralis, pars lateralis Nucleus dorsolateralis anterior, pars magnocellularis Nucleus suprarotundus Dorsolateral nucleus of OPT Nucleus superficialis parvocellularis	Nucleus rotundus

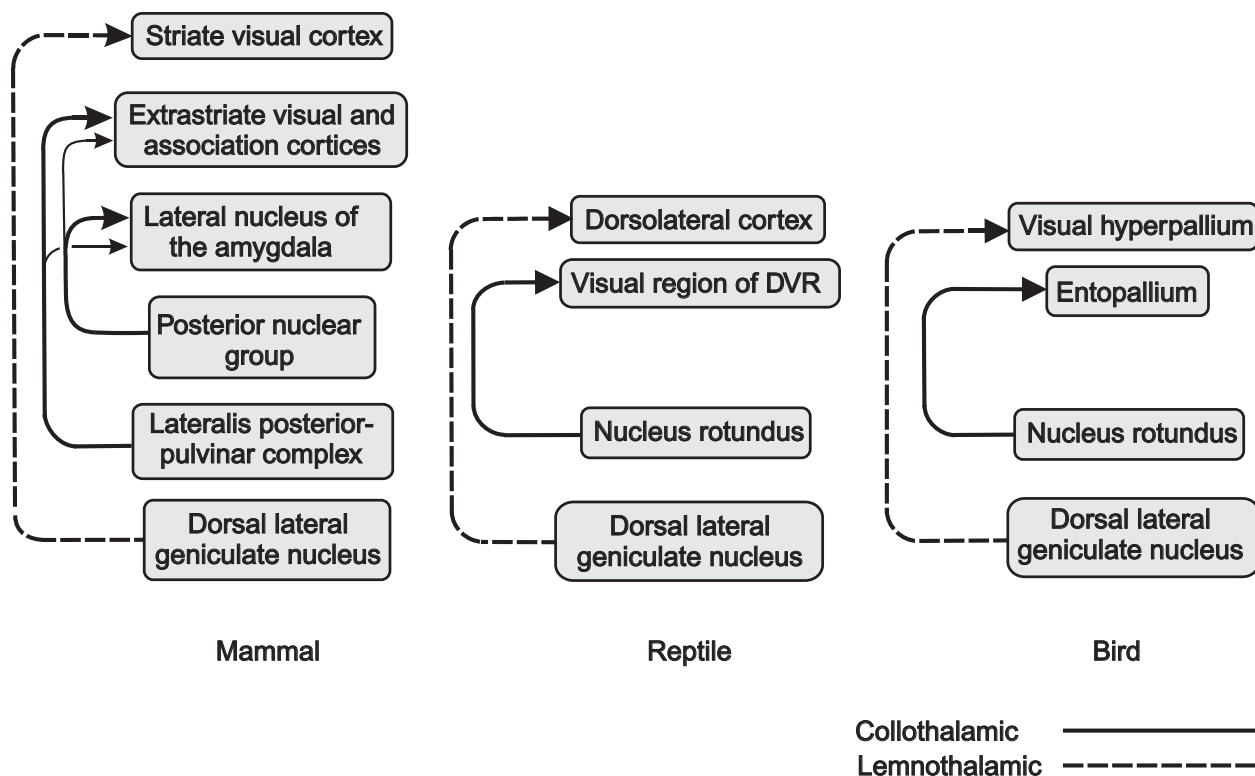


FIGURE 26-16. Summary of the collothalamic and lemnothalamic visual pathways to the telencephalon in three amniotes: a mammal, a reptile, and a bird.

dala. As discussed below, whether the nucleus rotundus of sauropsids is homologous to the lateralis posterior/pulvinar complex of mammals, to the visual components of the posterior nuclear group, or to both as a field homology is presently a matter of intense debate.

Lemnothalamic Visual Pathways

In reptiles and birds, the optic tract terminates in a cluster of nuclei, some of which appear to be within the dorsal thalamus. One or more of these nuclei were initially thought to correspond in some way to components of the dorsal lateral geniculate nucleus of mammals and were so named. To com-

plete the picture, in each case, a prominent, plate-like ventral division of the lateral geniculate nucleus was identified as well. More recent studies, however, have revealed that not all of the retinal target nuclei besides the ventral division are in the dorsal thalamus or send their efferents to the telencephalon; they therefore cannot all be considered as comparable to the dorsal division of the lateral geniculate nucleus of mammals. Some of these other nuclei, for example, send their efferents to the optic tectum and pretectum. Indeed, in reptiles, only one dorsal thalamic, retinorecipient nucleus sends its efferents to the telencephalon. This projection is ipsilateral. Because of the very different names assigned to the various dorsal thalamic visual nuclei in different animals, we recommend the use

of a more general name, the **dorsal lateral geniculate nucleus** for the lemnothalamic visual nucleus in nonmammalian amniotes (see Chapter 22). An alternative term still in use for birds is the **nucleus opticus principalis thalami**, or the **OPT complex**. In birds, the OPT (dorsal lateral geniculate)-telencephalic projection is bilateral.

As in mammals, in reptiles and birds, ascending axons from the lemnothalamus project to part of the dorsal pallium in the telencephalon. In turtles, this area is in the lateral part of **dorsal cortex** or **dorsolateral cortex** [see Fig. 26-17 (A)], and the corresponding cortical area in lizards is called the **pallial thickening** [see Fig. 26-17 (B)]. In birds, the termination of the lemnothalamic visual projections is in a region of dorsal of the telencephalon known as the **Wulst** (which means a bulge or bump in German). The Wulst was also previously referred to as the hyperstriatum, but this term now has been replaced with **hyperpallium** (see Chapter 19 for tables of the

new and earlier terminologies of the avian telencephalon). The region of the hyperpallium that receives the input from the visual lemnothalamus contains several layers of granule cells, which are similar in morphology and in some electrophysiological characteristics, including, retinotopic organization and columnar organization, to the granule cells of the striate cortex of mammals. These avian granule cells are thought to have evolved independently in birds, convergent with the similar granule cells in mammals, since such cell populations appear to be absent in reptiles. Also, there are fundamental differences in the embryological origin of the layers of the Wulst, now called pseudolayers, and of the layers of mammalian neocortex (see Fig. 25-13).

The layers within the visual hyperpallium that receive the lemnothalamic visual projections are the **hyperpallium densocellulare** (formerly the hyperstriatum dorsale), the **hyperpallium intercalatum** (formerly the hyperstriatum

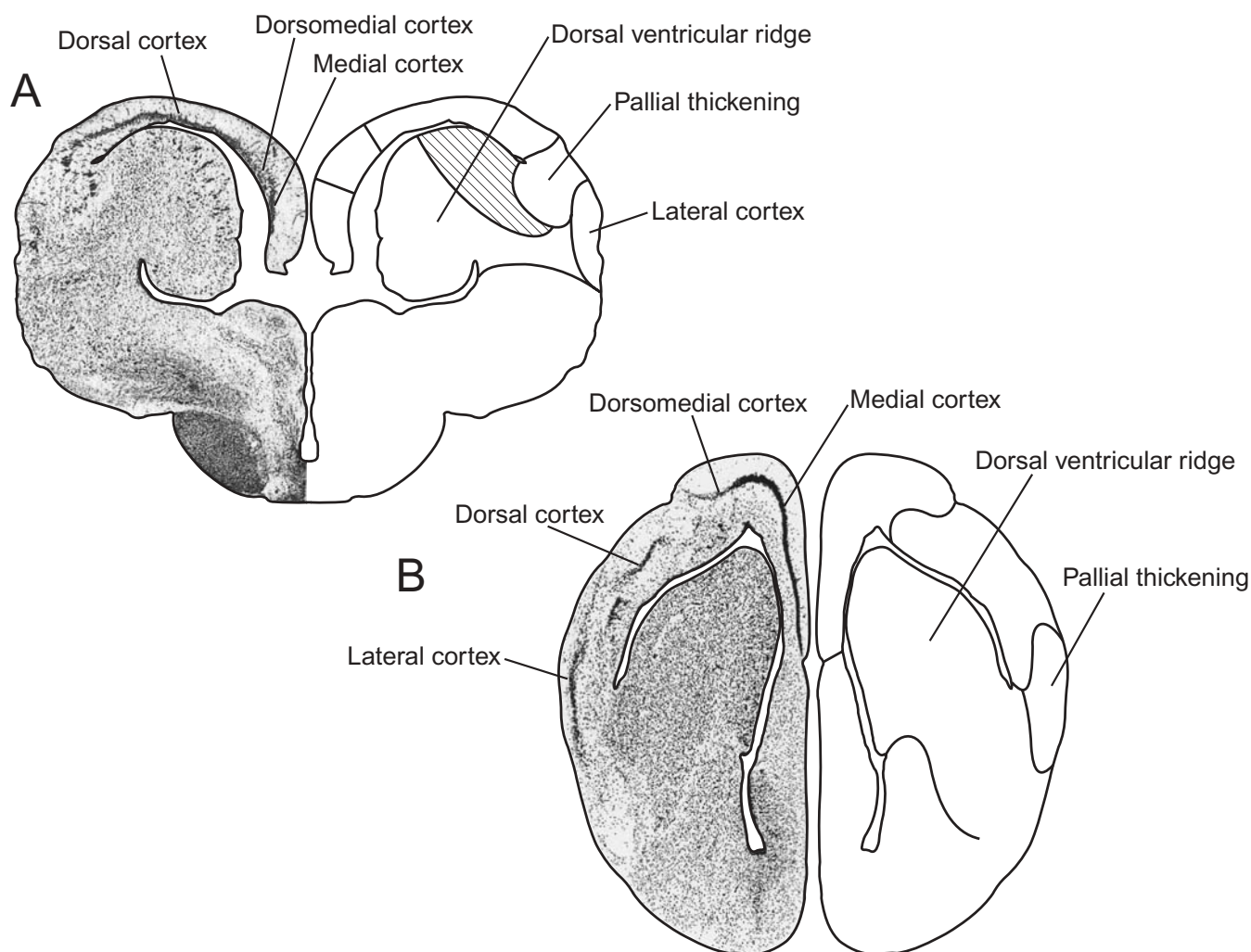


FIGURE 26-17. A: transverse hemisection with mirror-image drawing through the telencephalon of a turtle, showing the dorsal cortex and the visual part (diagonal lines) of the anterior dorsal ventricular ridge. Adapted from Balaban and Ulinski (1981) and used with permission of John Wiley & Sons. B: transverse hemisection with mirror-image drawing through the telencephalon of a lizard (*Tupinambis nigropunctatus*), showing the dorsal cortex. Adapted from Ebbesson and Voneida (1969). Used with permission of S Karger AG, Basel.

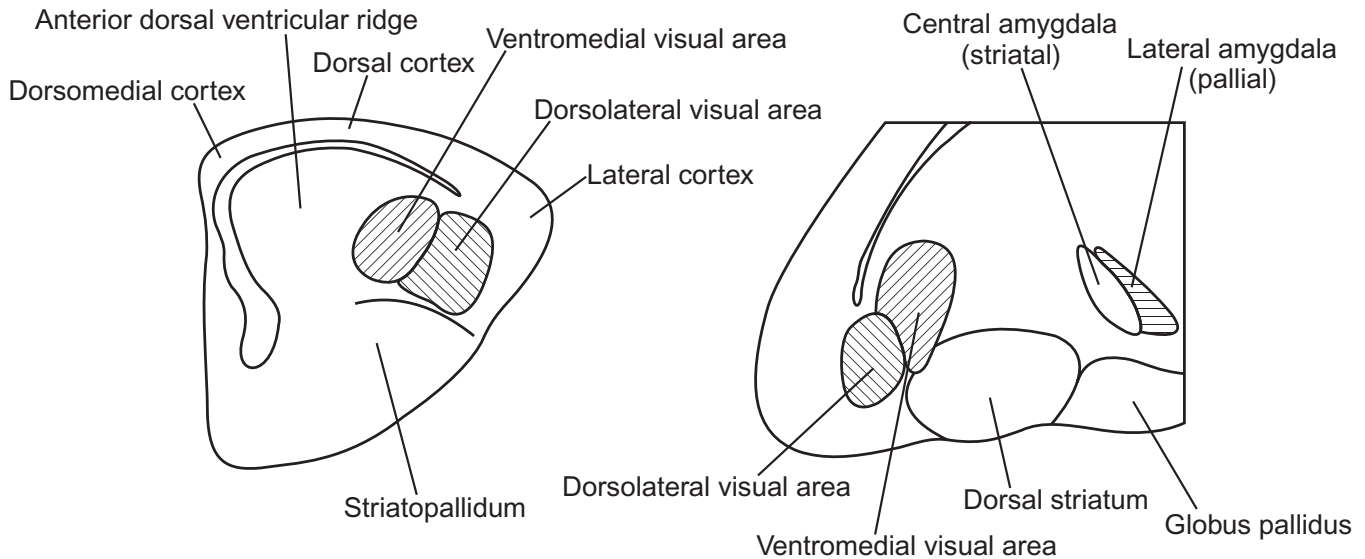


FIGURE 26-18. Left: drawing of a transverse hemisection through the right telencephalon of a lizard (*Psammotromus algrus*), showing the two visual areas (diagonal lines) of the anterior dorsal ventricular ridge. Right: drawing of a parasagittal section showing the latter two areas (diagonal lines) and an additional, more caudally lying pallial target, the lateral amygdala (horizontal lines). Adapted from Guirado et al. (2000) and used with permission of John Wiley & Sons.

intercalatus superior), and the **nucleus interstitialis hyperpalii apicalis** (formerly the nucleus intercalatus hyperstriati accessorium). These regions collectively are called the **visual hyperpallium** (Fig. 26-19). The densest lemnothalamic terminations within the visual hyperpallium are to the hyperpallium densocellulare and nucleus interstitialis hyperpalii apicalis. Like the striate cortex of mammals, the telencephalic components of the lemnothalamic visual pathway send their efferent projections to the optic tectum (superior colliculus), the lemnothalamic visual nucleus, and other targets of the optic tract.

Collothalamic Visual Pathways

Table 26-2 summarizes the collothalamic visual nuclei in mammals, reptiles, and birds. Here the nomenclature is relatively simple; in both nonmammalian groups, the collothalamic visual nucleus is called **nucleus rotundus**. In reptiles (Figs. 26-17 and 26-18), nucleus rotundus projects to a region known as the **visual area of the anterior dorsal ventricular ridge**. Although a single visual region within the anterior DVR has been assumed in most reptiles, recent work in the lizard *Psammotromus* has demonstrated the presence of two neighboring visual targets in the anterior DVR, as shown in Figure 26-18. An additional projection to a nucleus that lies in the posterior part of the DVR and has been identified as the lateral amygdala was also found in this reptile.

In birds (Figs. 26-19 and 26-20), the telencephalic target of nucleus rotundus is called the **entopallium** (formerly known as the ectostriatum core), which is a well-demarcated zone within the **nidopallium** (formerly the neostriatum), which is part of the anterior dorsal ventricular ridge. The entopallium is bordered by another region called the **perien-**

topallium (previously known as the peri-ectostriatal belt). The collothalamic fibers terminate in the entopallium, which in turn sends its axons to the perientopallium. This pathway comprises several separate projection systems: nucleus rotundus consists of several subdivisions, each projecting to a different region of the entopallium. In addition, another collothalamic nucleus, **nucleus triangularis**, which sits like a pointed hat atop nucleus rotundus, also receives tectal projections and projects to the entirety of the entopallium.

Efferents from the perientopallium are to other cell groups within the hyperpallium, ventrolateral mesopallium, and nidopallium regions of the telencephalon. In addition, direct projections from the perientopallium to the ventrolateral mesopallium as well as to the lateral striatum have been described.

Figure 26-20 shows a comparison of visual areas in an owl and an iguana. As in *Psammotromus*, two visual areas were found in the iguana, and they are surrounded by a belt region, similar to the perientopallium of the owl. Note also the very large and complex visual hyperpallium of the owl compared with the comparable region in a pigeon, shown in Figure 26-19. A large and well-developed visual hyperpallium is characteristic of the group of predatory birds known as raptors, which includes owls, hawks, and eagles.

EVOLUTIONARY TRENDS IN THE VISUAL SYSTEM OF AMNIOTES

An examination of the ascending visual pathways to the telencephalon in mammals, reptiles, and birds reveals a striking pattern of similarities, which almost certainly represents

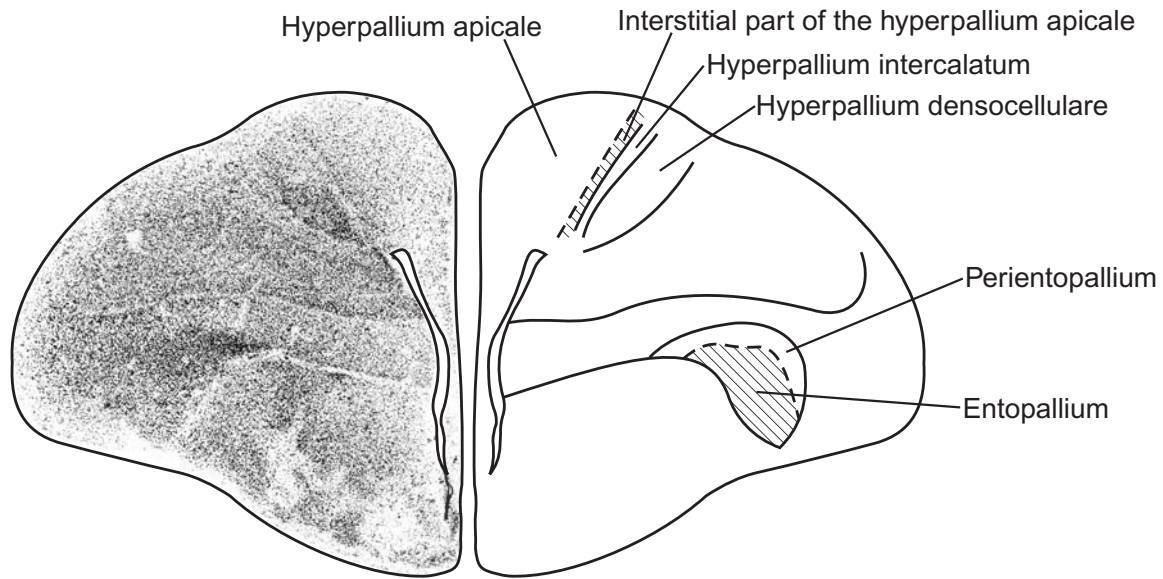


FIGURE 26-19. Transverse hemisection with mirror-image drawing through the telencephalon of a pigeon (*Columba livia*), showing the visual area of the anterior dorsal ventricular ridge, the entopallium (diagonal lines), and the parts of the visual hyperpallium. Adapted from Karten and Hodos (1967) with additional data from Karten and Hodos (1970). Used with permission of The Johns Hopkins University Press.

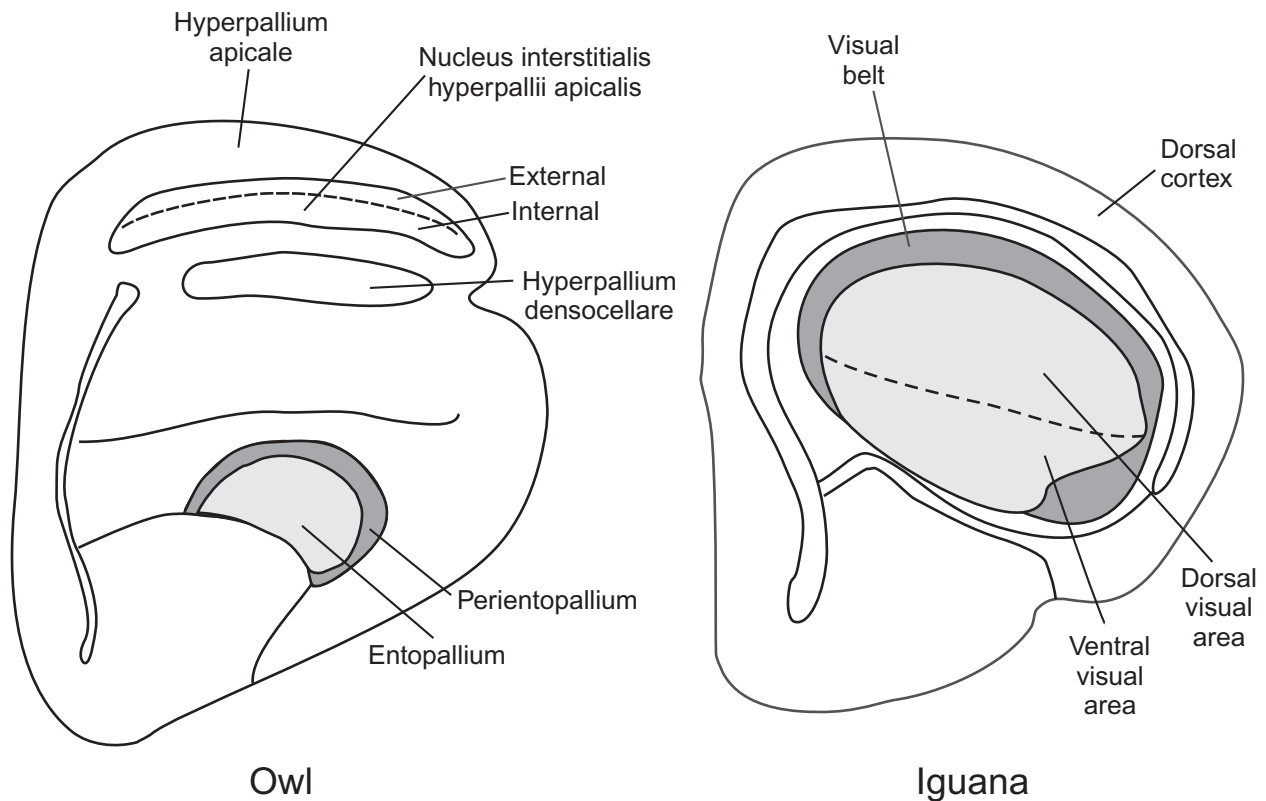


FIGURE 26-20. Drawings of transverse sections through the brain of an owl and an iguana showing the collothamic terminations in the telencephalon shaded in light gray. The two brains are not drawn to the same scale; the owl brain is much larger. In each species, the termination region is surrounded by a belt or shell region (shaded in dark gray). Note the large visual hyperpallium in the owl as compared to the comparable region in the pigeon (Fig. 26-19). Adapted from Manger, Slutsky, and Molnár (2002) and used with permission of John Wiley & Sons.

BOX 26-2. Functional Streams in the Avian Tectofugal Pathway

A key feature of the mammalian visual system is its organization into functional channels or streams based on electrophysiological studies and the behavioral effects of lesions to various regions of the visual cortex. Until recently, relatively little interest had been shown in the search for such channels in the visual telencephalon in nonmammals. Recent research into the avian tectofugal pathway, however, has suggested a greater segregation of function than had been previously appreciated. Although further details need to be added to the picture, a pattern is emerging that has many features in common with the mammalian, especially primate, visual system, as well as some important differences.

The avian nucleus rotundus consists of a number of morphological subdivisions, each of which projects to a distinct region within the entopallium. For some time, these regions were thought to be functionally equivalent. A number of recent physiological, anatomical, embryological, and behavioral studies have been suggesting otherwise.

Jorge Mpodozis and colleagues reported that pigeon retinal ganglion cells could be classified into at least five groups according to their conduction velocity. All five of these ganglion cell groups terminate in the optic tectum, but only the four groups with the highest velocity terminate in the dorsal lateral geniculate nucleus. Harald Luksch and colleagues also observed physiologically distinct categories of morphologically different neuron types in the optic tectum. These neurons, which also respond differently to their inputs from the retina, are the major source of afferents to nucleus rotundus.

Yong-Chang Wang, Shi-Ying Jiang, and Barrie Frost observed that neurons within the morphological subdivisions of nucleus rotundus have unique physiological specializations. Thus, cells in the dorsal anterior subdivision respond to the color of the stimulus, whereas those in the dorsal posterior division respond to an expanding or contracting stimulus (looming). Cells in the anterior central region respond to changes in the illumination of the stimulus, while those of the ventral zone seem to be most "interested" in small, rapidly moving stimuli.

From the anatomical perspective, Burkhard Hellmann and Onur Güntürkün observed that different classes of tectal neurons project to the individual subdivisions of nucleus rotundus. Antonio Laverghetta and Toru Shimizu observed a topographic projection from individual subdivisions of nucleus rotundus to the entopallium. In an embryological study, Tanja Becker and Christoph Redies described the expression of four different members of the cadherin class of cell adhesion molecules in nucleus rotundus. These molecules can be used as markers to identify neuronal populations during embryonic development. They found that each cadherin type was expressed in a different subdivision of nucleus rotundus, which suggests a functional segregation.

Finally, recent behavioral studies have shown that subdivisions of both nucleus rotundus and the entopallium have unique functional specializations. Angela Nguyen and collaborators studied the effects of selective lesions of the entopallium on a visual motion task and a static pattern discrimination task. They found that lesions of the anterior entopallium resulted in performance deficits in the pattern task but not in the motion task. In contrast, lesions of the posterior entopallium resulted in performance deficits in the motion task but not in the pattern task. Similarly, Laverghetta and Shimizu reported selective effects of lesions of the anterior division of nucleus rotundus on the discrimination of small, stationary targets.

More studies are required to determine the fine details of the physiological properties of these apparent functional streams and the effects of damage or interruption to them on visual behavior. Additional information should help to make clear the similarities and differences between the functional streams in mammals and birds.

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the heritage of these groups from their common ancestral, amniote stock. In addition, striking differences can be seen as well. Figure 26-16 shows a number of the common features of the pattern among mammals and reptiles in the collothamic and lemnothalamic visual projections to the telencephalon. The lemnothalamic visual route is from the dorsal lateral geniculate nucleus to the lemnothalamic visual part of the dorsal pallium, that is, the pallial thickening in lizards, lateral part of the dorsal cortex in turtles, visual hyperpallium in birds, and striate cortex in mammals. The collothamic visual route in sauropsids is from nucleus rotundus to the visual area of the anterior dorsal ventricular ridge, which in birds is known as the entopallium. In mammals, two collothamic visual pathways to pallium have been identified—one via the LP/pulvinar complex predominantly to extrastriate cortices and the other via the posterior nuclear group predominantly to the lateral nucleus of the amygdala.

Overlying this basic pattern of similarities are certain dramatic differences that have emerged between mammals and birds, possibly as a consequence of the development of substantial ipsilateral projections from the retina to the visual lemnothalamus in mammals. These differences include a dorsal lateral geniculate nucleus that is segregated into ipsilateral and contralateral subdivisions; P, M and K (X, Y, and W) channels; and a high degree of retinotopic organization. In mammals, the large number of representations of the visual field in the visual collocortices is unique among amniotes. The variation among the multiple representations suggests that multiple areas have been evolved independently in the various groups of mammals.

Birds, by a process of convergent or parallel evolution, have also independently evolved certain similarities to mammals: multiple components of the visual lemnothalamus (dorsal lateral geniculate nucleus) as well as granule cells and a columnar organization in their dorsal pallial equivalent to striate cortex, the visual hyperpallium. Some birds with an extreme frontal position to their eyes, such as owls, have a highly developed binocular organization to the visual hyperpallium. A major difference, however, between the avian and mammalian visual systems is that the mammalian system has developed ipsilateral retinal projections to the dorsal thalamus to an extent unparalleled among other vertebrates, whereas the avian visual system is virtually contralateral from the retina to the lemnothalamic diencephalon but bilateral from the diencephalon to the visual Wulst. Among all vertebrate groups, birds have the best color vision as well as outstanding visual acuity that would be the envy of any mammalian predator.

Still unresolved is the comparison of collothamic pathways between sauropsids and mammals. Whether the sauropsidian nucleus rotundus is homologous to the mammalian LP/pulvinar or to the posterior nuclear group or to both remains to be elucidated. The similarities of the two collothamic pathways in mammals make it difficult to single out either one to the exclusion of the other as a clear homologue of the rotundal pathway. Both LP/pulvinar and the posterior nuclear group exhibit multiple features in common, as listed here: 1) Developmental evidence suggests that they both arise embryologically from a single pronucleus, initially identified by Jerzy Rose in his study of the rabbit diencephalon and named by him as the dorsal pronucleus. 2) They both receive visual input

relayed from neurons within the optic tectum; that this input arises from different tectal layers may not be of import, since the laminar origin of input to the clearly homologous dorsal lateral geniculate nucleus also varies markedly across amniotes (see Chapter 18). 3) They both give rise to a major projection to one of two targets—extrastriate visual and association cortices or the lateral nucleus of the amygdala—and to a minor projection to the other of these two targets. 4) They both also project to both the caudate-putamen (dorsal striatum) and to the lateral (external) segment of the globus pallidus. In contrast, a difference is that the posterior nuclear group projects to the claustrum (dorsal claustrum, or claustrum proper), while LP/pulvinar does not. However, this difference is not one that assists in determining the relationship of either mammalian collothamic visual pathway to the pathway through nucleus rotundus in sauropsids. Rather, the extensive similarities in the two mammalian pathways, including the common embryological anlage for LP/pulvinar and the posterior nuclear group, may be evidence of a field homology of both of them to the single nucleus rotundus. Should either one of the two pathways in mammals prove to be the single homologue of the rotundal pathway, the evolution of the other pathway in mammals still would remain to be explicated.

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Somatosensory and Motor Forebrain in Amniotes

INTRODUCTION

In this chapter, we will discuss the somatosensory (or somesthetic) forebrain and the motor forebrain of mammals, reptiles, and birds. The somatosensory worlds of these animals consist of the consequences of mechanical and thermal stimulation of the external and internal surfaces of the body and head. These include the heating, cooling, indentation, and stretching of surfaces, the bending of joints, the stretching of tendons and muscles, and other consequences of the activity of the musculoskeletal system. In addition, the bending of hairs, feathers, and scales also serve as important indicators of events in the external environment. Chapter 2 summarized many of these stimuli and their somatosensory receptors.

As in Chapter 26, most of our discussion will center on mammals because they have the most elaborate telencephalic representations of these systems and because they have been more intensively studied than nonmammalian amniotes. Many of the principles of organization that we saw in the visual cortex of mammals will apply as well to their somatosensory and motor cortices. These include topographic organization, multiple representations, and collothalamic and lemnothalamic input. The topography that is described in this chapter is that of the body and head of the animals, that is, a **somatotopic organization**. Because of the similarity of their somatotopic organizations, the somatosensory and motor systems are convenient to discuss in the same chapter.

Both the extent and the details of the somatotopic organization of the somatosensory regions and the motor regions of the telencephalon can be measured physiologically, but by different methods. Somatosensory mapping is performed by

placing a recording electrode on (or in) the telencephalon and then stimulating various body parts by touch, temperature, pressure, or other stimuli and noting those body regions at which the stimulation affects electrical activity at the telencephalic location. Motor mapping also uses a telencephalic electrode, but in this instance it is a stimulating electrode. The experimenters observe which regions of the body move when a particular telencephalic site is stimulated electrically. The resulting maps generally are of the contralateral body half because of the crossing, or **decussation**, of the ascending secondary sensory axons on route to the dorsal thalamus and of the descending motor pathways on route to the spinal cord, whether directly or via relay through parts of the brainstem. Both of these types of physiological maps are then correlated with cytoarchitecture, areas of termination of thalamic input, and areas of origin of descending pathways to the brainstem and spinal cord to develop a complete picture of the system. An important consideration in evaluating these maps is that the size and shape of the map can change according to the methods used to elicit it; for example, the size and shape of the maps can be affected by the type and depth of anesthesia used or by the type of recording or stimulating electrode. Such maps can also be affected by experience, such as the removal of a body part. In general, however, a reasonably good congruence exists between maps obtained by different methods.

THE SOMATOSENSORY AND MOTOR FOREBRAIN OF MAMMALS

One of the defining characteristics of mammals is the presence of hair. When we think about hair, we tend to think of

temperature regulation and protection. Hairs, however, also have an important sensory function (see Chapter 2) in that they can be deflected by objects near to the body surface. The hair follicle receptors at the bases of the hairs then report the fact of this close encounter with something to the somatosensory system. Hair-covered skin, however, like a gloved hand, cannot be used for determining the fine surface details of an object. Direct contact between the skin itself and the objects being inspected allows for greatly increased sensitivity to fine detail. The hairless skin on the palms of hands and forepaws and on the soles of feet and hindpaws is known as **glabrous** skin and has a high degree of sensitivity for touch and fine detail. Mammals with a highly developed sense of touch typically have separate representations of the hairy and glabrous regions of the skin in their somatosensory cortices.

The Ventral Tier Nuclei of the Dorsal Thalamus

Anatomists sometimes find it convenient to divide the dorsal thalamus into two layers or tiers (as in the tiers of a stadium). A **dorsal tier** and a **ventral tier** of the dorsal thalamus have thus been recognized (see Chapter 22). The nuclei of the ventral tier have names that begin with “ventralis,” such as ventralis anterior, ventralis lateralis, ventralis posteromedialis, or ventralis posterolateralis. The ventral tier nuclei have in common that they are the somatosensory and motor nuclei of the dorsal thalamus. Note that the *ventral tier* of the dorsal thalamus should not be confused with the *ventral thalamus*, which is an entirely different structure, discussed in Chapters 19 and 24.

Just as the somatosensory cortex and the motor cortex are located more or less in close proximity to each other, so are their associated dorsal thalamic nuclei. The more anterior of the ventral tier nuclei have their principal connections with the cortical components of the motor system as well as with non-cortical components, such as the cerebellum, corpus striatum (i.e., the dorsal striatum and dorsal pallidum), and substantia nigra. The more caudal group of ventral tier nuclei receives the ascending somatosensory axons from the spinal cord, the dorsal column nuclei, and the trigeminal nuclei of the brainstem.

Somatosensory Lemnothalamus

The somatosensory nuclei of the dorsal thalamus are known as the **ventrolateral** or **ventrobasal complex**. This group of nuclei is located ventral to the lateralis posterior/pulvinar complex that we encountered in the previous chapter and consists of two principal nuclei: **nucleus ventralis posteromedialis (VPM)** and **nucleus ventralis posterolateralis (VPL)**. Nucleus ventralis posterolateralis receives its input from the somatosensory cell groups in the dorsal horn of the spinal cord and also from the dorsal column nuclei (nuclei gracilis and cuneatus) via the **medial lemniscus**, which thus carries information about somatosensory stimulation of the body. Nucleus ventralis posteromedialis is the comparable thalamic nucleus for somatosensory projections from the head and face regions. It receives ascending axons from the sensory nuclei of the trigeminal nerve in the pons. Together, nuclei

ventralis posterolateralis and ventralis posteromedialis contain a complete, somatotopically organized representation of the body, including the head and face. In primates, several additional components of the ventrolateral complex exist as well. Within the ventrolateral complex are a superior region that receives input from muscle and joint receptors, a central region that contains a somatotopic representation of both slowly adapting and rapidly adapting skin receptors, and an inferior region that receives input from the spinothalamic tract with pain and temperature information. The ventrolateral complex sends its efferents to the two major areas of somatosensory cortex, **somatosensory area 1** and **somatosensory area 2**, often abbreviated as **S1** and **S2**, or **SI** and **SII** by those who prefer Roman numerals.

Related to the ventrolateral complex in terms of the organization of its afferent and efferent projections is a more caudal nucleus, the **medial part of the posterior nuclear group (Pom)**. The Pom receives somatosensory lemniscal projections from the dorsal column nuclei in the caudal medulla. In turn, Pom projects to somatosensory cortex (S2). We thus include Pom with the ventrolateral complex in the somatosensory lemniothalamus.

Somatosensory Collothalamus

Caudal to the ventrolateral complex is another group of nuclei—the **posterior nuclear group**, which includes the **nucleus limitans** and the **suprageniculate nucleus**. The suprageniculate/limitans nuclear complex receives input from the somatosensory-multisensory part of the tectum, that is, the superior colliculus, of the midbrain, which receives ascending axons from the dorsal column nuclei. The suprageniculate/limitans complex thus constitutes the collothalamic somatosensory thalamus. The efferents of the suprageniculate/nucleus limitans complex are to neocortex located in the posterior region of the insula. This **posterior insular cortex** is comparable to extrastriate visual cortex of mammals in that it is the target of a collothalamic rather than a lemniothalamic pathway.

Motor Lemnothalamus

The rostral (or oral) end of the ventral tier comprises the motor division of the dorsal thalamus. Unfortunately, this is another of those regions with confusing nomenclature due to subdivisions into separate nuclei of nuclei that originally were thought to be a single entity and due also to the differences in thalamic organization between species that are correlated with differences in cortical organization. The motor nuclei of the ventral tier are considered to be part of the lemniothalamus due to their lemniscal-like inputs from motor related structures, that is, direct afferent projections, without relay through the roof of the midbrain, and their projections to motor cortices (M1 and M2). We will briefly digress to note that if motor collothalamic pathways exist, one might consider the suprageniculate/limitans complex in this context, in that the somatosensory part of the superior colliculus receives motor-related input from the substantia nigra and via relay through the pretectum (see Chapters 17 and 24). This pathway thus could be considered motor as well as sensory.

Two points should be kept in mind about the motor thalamus. The first is that, unlike the motor cortex, the motor thalamus has no direct connections with motor nuclei of the brainstem or spinal cord; it is “motor” only in the sense that its major connections (both afferent and efferent) are with motor cortex, the cerebellum, and the striatum. It thus serves as a major input pathway to motor cortex as well as being an important feedback pathway from cortex to thalamus and back to cortex. The second point is that the description of motor thalamus presented here is based largely on studies of cats and primates, which are the subjects of the overwhelming majority of research studies in this area and which seem to have some of the most elaborately developed forebrain motor systems.

The most rostral component of the motor thalamus is **nucleus ventralis anterior (VA)**, which is involved in pathways associated with the noncortical components of the motor system: the basal ganglia (especially the internal segment of the globus pallidus) and the pars reticulata of the substantia nigra of the midbrain (see Chapter 24). Moving caudally, we next encounter **nucleus ventralis lateralis (VL)**, which receives axons from the cerebellum by way of a relay through the deep cerebellar nuclei. Still farther caudally, we come to **nucleus ventralis posterolateralis (VPL)**, which also receives cerebellar input via the deep cerebellar nuclei.

The alert reader may now be justifiably confused, for the moment, since we just stated above that VPL is part of the *somatosensory* system. The problem lies in the fact that VPL is one of those instances of a nucleus that was originally thought to be a single structure and was later deemed by some workers to be two separate entities that were difficult to separate on cytoarchitectonic criteria alone. Thus, anatomists now commonly refer to a **nucleus ventralis posterolateralis, pars oralis (VPLo)**, which is the motor component of VPL, and a **nucleus ventralis posterolateralis, pars caudalis (VPLc)**, which is the somatosensory component. To make matters worse, most scientists who study the somatosensory system refer to VPLc simply as VPL, whereas those who study the motor system usually distinguish the motor component, VPLo, from the somatosensory component, VPLc. Furthermore, some workers consider VPLo actually to be a subdivision of nucleus ventralis lateralis, rather than of nucleus ventralis posterolateralis. A small consolation for this nomenclatural confusion may be taken from the fact that, like the motor/somatosensory arrangement in neocortex, the motor components of the ventral tier are rostral (oral) to all of the somatosensory components, which facilitates remembering that VPLo is motor while VPLc is somatosensory.

One additional nucleus remains to be added to the cast of characters in the motor thalamus; this is a collection of neurons situated medial to VPLo and known by the slightly mysterious name of **nucleus X**. Nucleus X, along with VPLo, may also be a subdivision of nucleus ventralis lateralis.

Afferents to Somatosensory Cortex

Figure 27-1 summarizes the lemnothalamic and collothalamocortical afferents to the somatosensory cortex. As shown in this figure, somatosensory axons from receptors for pain, touch, temperature, and other somesthetic sensations from the body enter the dorsal horn of the spinal cord. Some lemnothalamic

axons of dorsal horn cells pass directly to the ventrolateral complex of the dorsal thalamus and terminate in VPL (i.e., VPLc), which contains the representation of the body. Other somatosensory axons from the periphery project to the dorsal column nuclei from which lemnothalamic efferents also pass to VPL. The corresponding somatosensory axons from receptors in the face and head regions of the body enter by way of the three branches of the trigeminal nerve in the pons and terminate in the principal and descending nuclei of the trigeminal nerve. Efferent axons of these trigeminal nuclei join those from the spinal cord and medulla to terminate in VPM, which is specialized for the somatotopic representation of the head. The efferents of the ventrolateral complex are to S1 and S2. A third lemnothalamic pathway originates in the dorsal horn. These axons terminate in the medial part of the posterior nuclear group (Pom). The efferent axons of Pom project to S2.

Also shown in Figure 27-1 is the collothalamocortical somatosensory pathway. This pathway arises in the dorsal column nuclei with its first termination in the somatosensory-multisensory region of the midbrain tectum, that is, the superior colliculus. From there, tectothalamic axons project to the suprageniculate (SG)/nucleus limitans group in the posterior thalamus, the efferents of which terminate in the posterior insular cortex.

Efferents of Somatosensory Cortex

Both S1 and S2 are the major sources of efferents from the somatosensory cortex, with S4 (or its equivalent) also serving as an additional output route in those mammals that possess a fourth representation of the body. Figure 27-2 summarizes the efferents of S1, which may be divided into two categories: **cortico-cortical** and **descending**. The cortical targets of S1 are motor cortex, S2, and the posterior parietal cortex. The descending efferents of the somatosensory cortex are to the corpus striatum and to the brainstem and spinal cord components of the somatosensory system: the dorsal horn of the spinal cord, the dorsal column nuclei, and the ventrolateral complex.

The efferents of S2 and S4 are summarized in Figure 27-3. The efferents of S2 are to S4 (when present), as well as to motor cortex, posterior parietal cortex, frontal cortex—including the **frontal eye fields** (which are a region of the frontal lobe that are specialized for movements of the eyes), the **perirhinal cortex** (the area around the rhinal fissure in the ventrolateral frontal lobe), and the pontine nuclei. The projections of S4 are more limited and are to motor cortex, posterior parietal cortex, and the frontal eye fields, which will be discussed below. If we compare the afferent and efferent connections of S2 in Figures 27-1 and 27-3, we see that S2 has a central position in the distribution of somatosensory information, with inputs from S1, posterior parietal cortex, the thalamic ventrobasal complex and Pom, and with efferents to a variety of cortical and subcortical areas.

Pain Pathways

Ascending Pain Pathways. Three main pathways carry information about pain to the cerebrum: the lateral spinothalamic tract, the spinoreticular pathway, and the spinomesencephalic

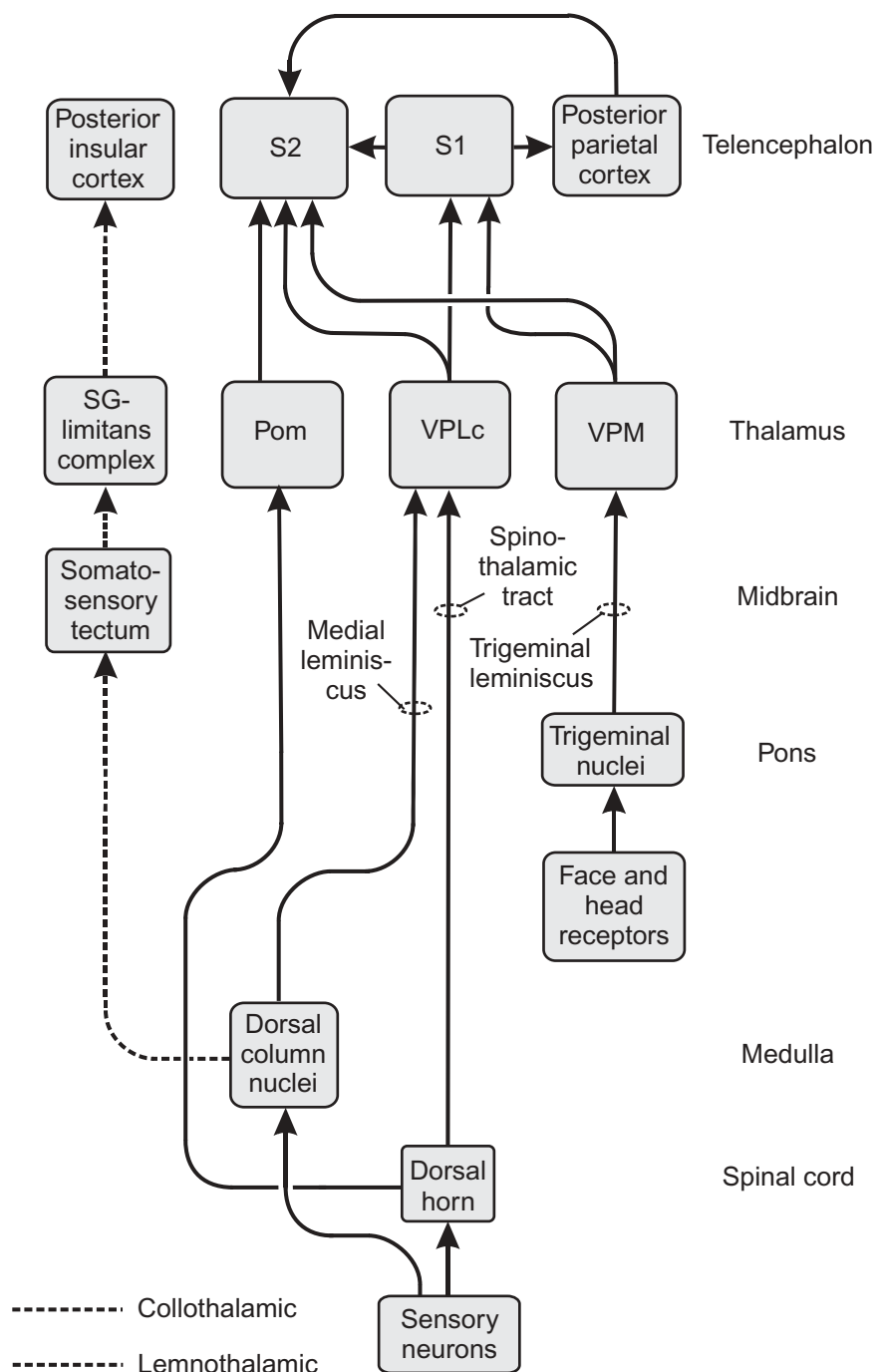


FIGURE 27-1. A schematic representation of the lemnothalamic and collothalamic somato-sensory pathways in mammals. Abbreviations: SG, supragenicular nucleus; Pom, medial division of the posterior nuclear group; VPLc, nucleus ventralis posterolateralis, pars caudalis; VPM, nucleus ventralis posteromedialis.

pathway. In addition, the pain system has an elaborate descending pathway that is involved in the modulation of pain. The lateral spinothalamic tract, which is the fast, highly localizable pathway from the body, is shown in Figure 27-1. The trigeminal lemniscus carries similar sensations from the head. Figure 27-4 depicts the remaining two pathways, which are more

slowly conducting, more diffuse in their localization of pain, and are concerned with the emotional aspects of pain. The spinoreticular pathway, shown with solid lines, passes from the spinal cord to the reticular formation of the hindbrain, in particular, the locus coeruleus, the nucleus reticularis gigantocellularis, the nucleus reticularis lateralis, and the raphe group

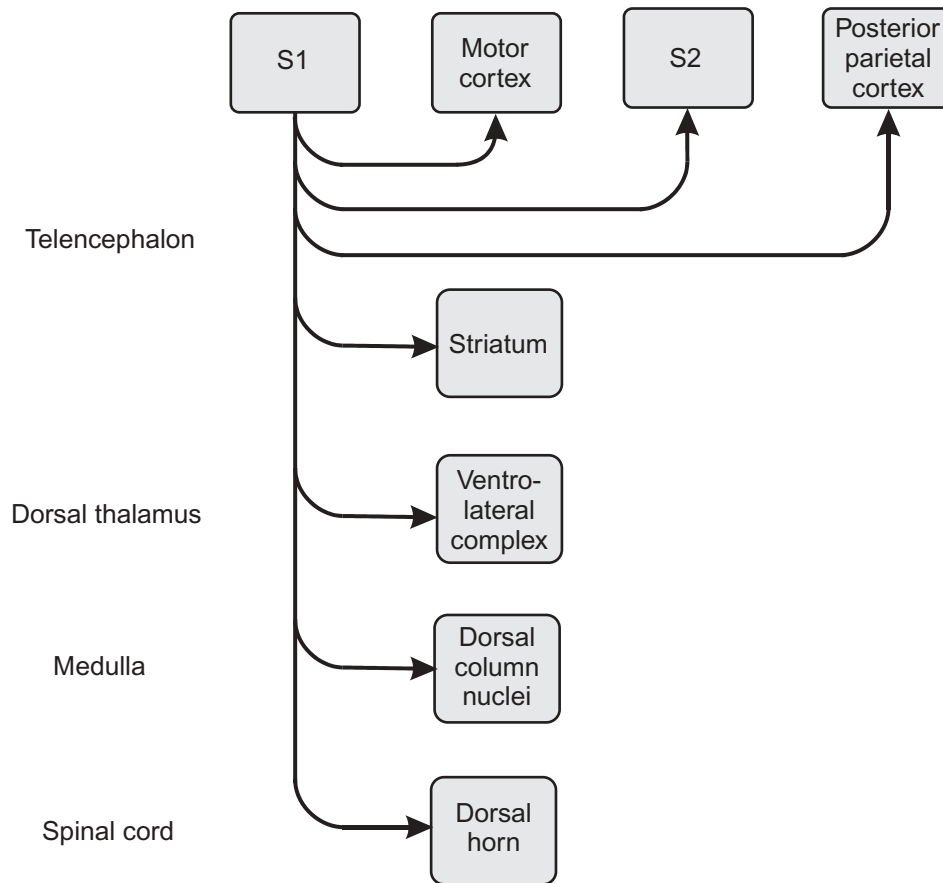


FIGURE 27-2. Schematic representation of the efferents of somatosensory cortical area S1.

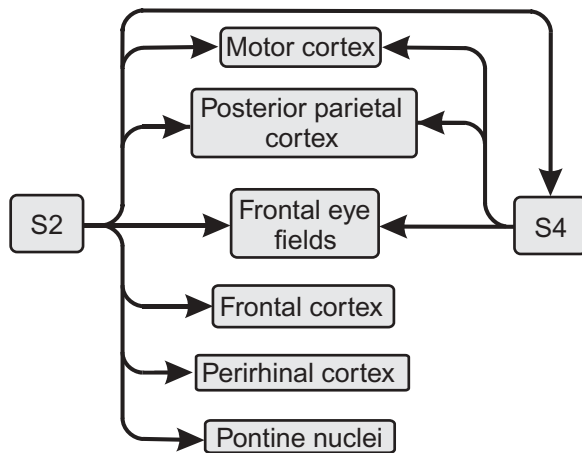


FIGURE 27-3. Schematic representation of the efferents of somatosensory cortical areas S2 and S4.

(see Chapter 13). The pathway continues rostrally, with some terminations (not shown in the figure) in the periaqueductal gray of the midbrain, and terminates in three thalamic areas: the centromedian and parafascicularis group, the nucleus centralis lateralis, and the medial part of the posterior group (see Chapter 22). The efferents of centromedian/parafascicularis

route terminate in the frontal cortex, the efferents of the centralis lateralis nucleus are to the limbic lobe, in particular, the cingulate cortex and amygdala, and the posterior group efferents are to the insula. All of these telencephalic regions (see Chapter 30) have been implicated in aspects of emotional behavior.

The spinomesencephalic route, shown as broken lines, consists of efferents from the spinal cord to the periaqueductal gray of the midbrain and the hypothalamus. Both the periaqueductal gray and the hypothalamus are involved in emotional behavior, the latter by way of its control over both the endocrine system and the visceral motor system (see Chapter 23). The pathway continues from the periaqueductal gray to the same group of thalamic and telencephalic targets as does the reticulospinal route. Both pathways also have connections with S1 and S2 for the localization and conscious perception of pain.

Descending Pain Pathways. Figure 27-5 illustrates the major descending pain pathways. These pathways modulate the intensity of perceived pain by means of a variety of inhibitory and gating mechanisms. As the figure shows, the descending projections are from S1, S2, and the frontal cortex to nuclei of the spinothalamic, spinoreticular, and spinomesencephalic pathways such as the periaqueductal gray, the reticular formation, especially the raphe magnus nucleus, a major source of

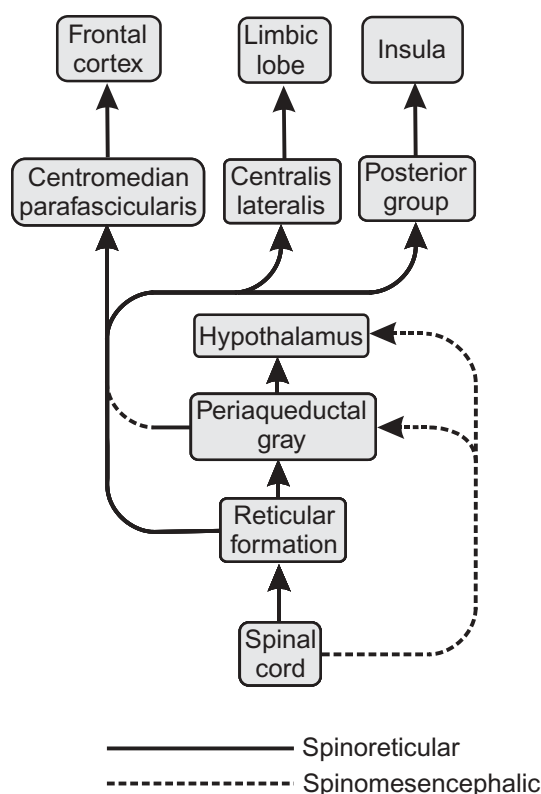


FIGURE 27-4. The slow pain pathways to the somatosensory cortex: the spinoreticular and the spinomesencephalic pathways. Adapted from Haines (2002).

serotonin and opioid neuromodulators, and to the spinal cord. Finally, descending axons from the limbic structures of the telencephalon pass to the hypothalamus, which participates in a cascade of connections to the periaqueductal gray, to the hindbrain reticular formation, and the spinal cord.

Neuroactive Substances and Pain. Among the many neurotransmitters and neuromodulators that have been found, components of the pain system of the brain and spinal cord are the excitatory neurotransmitter glutamate, as well as substance P, neurokinins A and B, calcitonin gene-related peptide, vasoactive intestinal polypeptide, and somatostatin. The principal inhibitory neurotransmitter is GABA. The substances that are involved in the descending, pain-control pathways are norepinephrine, serotonin, and various opioids.

Somatotopic Organization

A principle of central nervous system organization that has emerged in many of the preceding chapters is topographic organization. This principle can be observed in its most dramatic form in somatotopic maps. Moreover, the greater use an animal makes of a sensory or motor system, the greater the amount of neural tissue that is dedicated to processing the functions of that system. Thus, those body parts that have the greatest sensitivity have the largest representation in the somatosensory cortex, and those body parts that have the

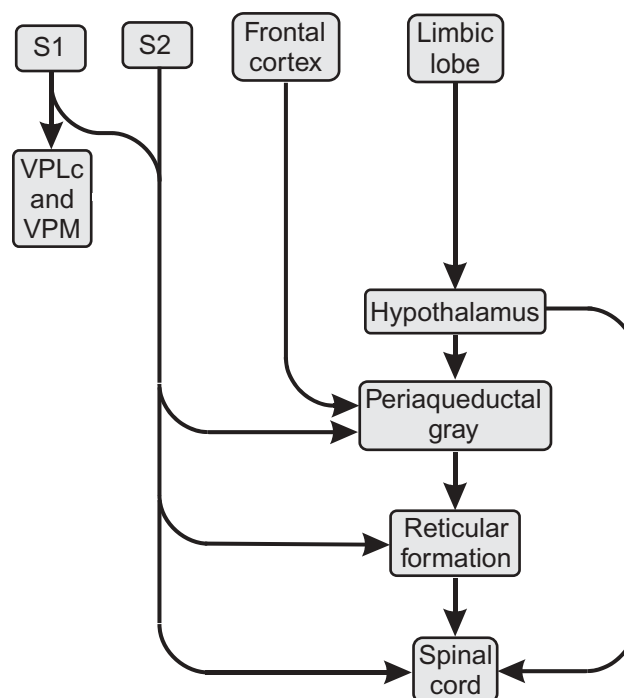


FIGURE 27-5. Descending pain pathways. Adapted from Haines (2002). Abbreviations as in Figure 27-1.

greatest dexterity of movement have the biggest representation in the somatotopic, cortical motor map. The structure with the largest representation on the somatosensory map may not necessarily have the largest representation on the motor map, however. For example, in humans, the hand and especially the fingers are very well represented in both the somatosensory and motor maps. In the somatosensory map, the index finger has the largest amount of cortex dedicated to it, whereas in the motor map, the greatest representation is that of the thumb. Figure 27-6 shows a map of the somatosensory cortex and the motor cortex of a human at the top. The heavy line that separates them is the central sulcus. The broken lines show the planes of section of each of the cross-sectional maps shown below, one for the motor cortex and one for the somatosensory cortex. Each of the lower maps begins at the left on the medial surface of the cerebral hemisphere, continues around the lateral surface, and curls down into the depths of the lateral sulcus. Note that, although the somatosensory and motor maps are not identical, there is a high degree of similarity between them. Note also the large areas of cortex in each devoted to the hand, fingers, and thumb, as well as to the lips, tongue, and throat, in contrast to the relatively small areas for relatively insensitive and immobile regions, such as the trunk and hip.

The close alignment of the somatosensory map and the motor map might lead one to conclude that the two maps have a high degree of interconnectedness. In fact, relatively few direct connections between somatosensory cortex and motor cortex have been reported. Instead, the principal efferent pathways from somatosensory cortex are back to the regions of the ventrolateral complex from which they originated, as well as

BOX 27-1. What is "Neo" About the Neospinothalamic Tract?

Pain is unusual among the senses because it has an emotional component as well as a sensory component. The sensory component tends to be sharply localizable and rapid in its onset after the initiation of the stimulus. The emotional component tends to be slower in onset and more diffuse in its localizability. These two aspects of pain are associated with different pathways within the central nervous system. Fast, highly localizable pain is a function of the lateral spinothalamic tract and its trigeminal partner, the trigeminal lemniscus, which are classical lemniothalamic pathways, the ventrobasal thalamic complex, and S1 and S2. Slow, diffuse, emotional pain is associated with the reticular formation, the periaqueductal gray, the hypothalamus, various nonspecific thalamic nuclei (see Chapter 22) and the limbic telencephalon (see Fig. 27-4). Two terms that are widely used in the pain literature to describe these pathways are the "**neospinothalamic**" for the spinothalamic, fast-pain route and "**paleospinothalamic**" for the spino-reticular-mesencephalic, slow-pain route.

Many writers on the subject of pain pathways make the undocumented assertion that the so-called "neospinothalamic" pathway is of recent phyletic origin (meaning in mammals according to some authors or in primates according to others), whereas the "paleospinothalamic" route is of ancient origin. This distinction is another example of *scala naturae* thinking (see Chapter 5).

A survey of the comparative literature on direct spinothalamic pathways in vertebrates gives a mixed picture. Although examples of direct (i.e., fast) projections from the spinal cord to the thalamus can be found in all classes of vertebrates, they are also absent in a number of the anamniote species that have been studied. Among the amniotes, direct spinothalamic pathways of the sort described in this chapter have been found in birds and mammals. The reptile picture is somewhat uncertain; although direct spinothalamic projections have been reported in various reptiles, the opinion of some investigators is that they more closely resemble spinal projections to the ventral thalamus than to the dorsal thalamus. Is the neospinothalamic pathway a phyletically "new" pathway? The answer depends on which group of vertebrates is under discussion. Because this pathway appears to be widely distributed among mammals, and mammals predate both birds and reptiles in evolutionary history, the pathway is not "new" among amniotes. Is it "new" among mammals? The

answer is that it probably is, although not necessarily new in an absolute sense. This pathway appears to have evolved independently a number of times in widely divergent groups; one cannot say with certainty whether it was present or not in ancient lineages.

Looking at the problem another way, one could ask "Is the paleospinothalamic pathway more ancient the neospinothalamic pathway?" The answer is "probably" since the spino-reticular pathway appears to be present in all vertebrates that have been examined thus far, whereas the spinothalamic pathway is found only intermittently, if at all, in anamniotes and not with any great certainty in reptiles.

Because of the vagaries of descriptors such as "neo-" and "paleo-," we suggest that these terms not be used at all in this instance. Less ambiguous terms would be "the fast pain" pathway and the "slow pain" pathway, or the "spinothalamic" pain pathway and the "reticulo-mesencephalic" pain pathway.

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some projections to the striatum, the dorsal column nuclei, and the spinal cord.

In general, animals that use their face and snout region to explore the environment, such as pigs and eulipotyphlans (formerly known as "insectivores"), have large representations of these areas. Likewise, bats have a large cortical area dedicated to sensations from the wings, and raccoons (see Box 2-3,

Fig. 1B) and nonhuman primates have an exceptional representation of the hand area. In such maps, each individual digit or each individual palm pad has its own dedicated region of cortex.

Overlap and Separation of Somatosensory and Motor Maps. A frequently observed mammalian pattern is for the

somatosensory map to abut the motor map or to have a strip of neocortex separating the two maps. This intermediate strip is sometimes known as “silent” cortex because it does not respond to mechanical or thermal stimulation of the body, and electrical stimulation of this strip does not result in movement of a body part. Examples of this intermediate strip may be seen in the

guinea pig and bushbaby (a small primate) in Figure 27-7. A number of exceptions to this rule have been described, however. In the platypus, for example, somatosensory and motor cortices have been reported to partially overlap each other, with at least two-thirds of motor cortex being in the somatosensory area and about one-quarter of somatosensory

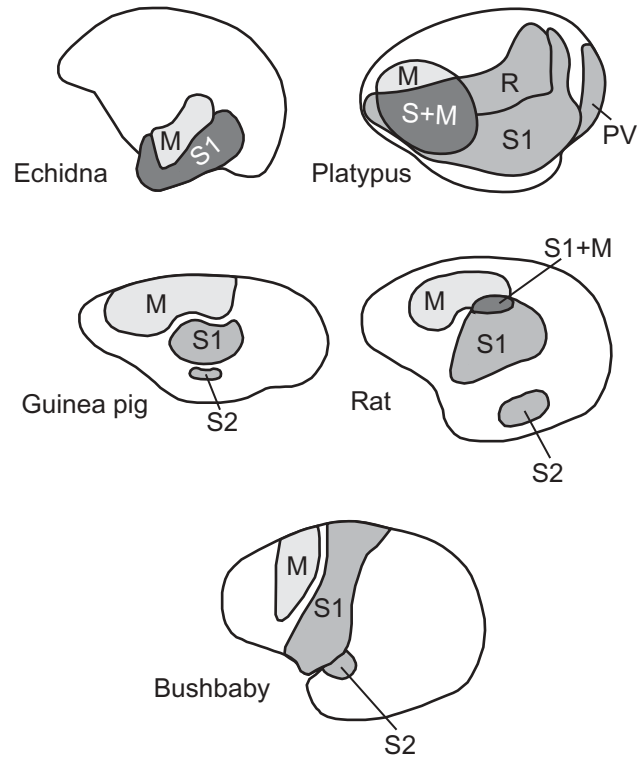
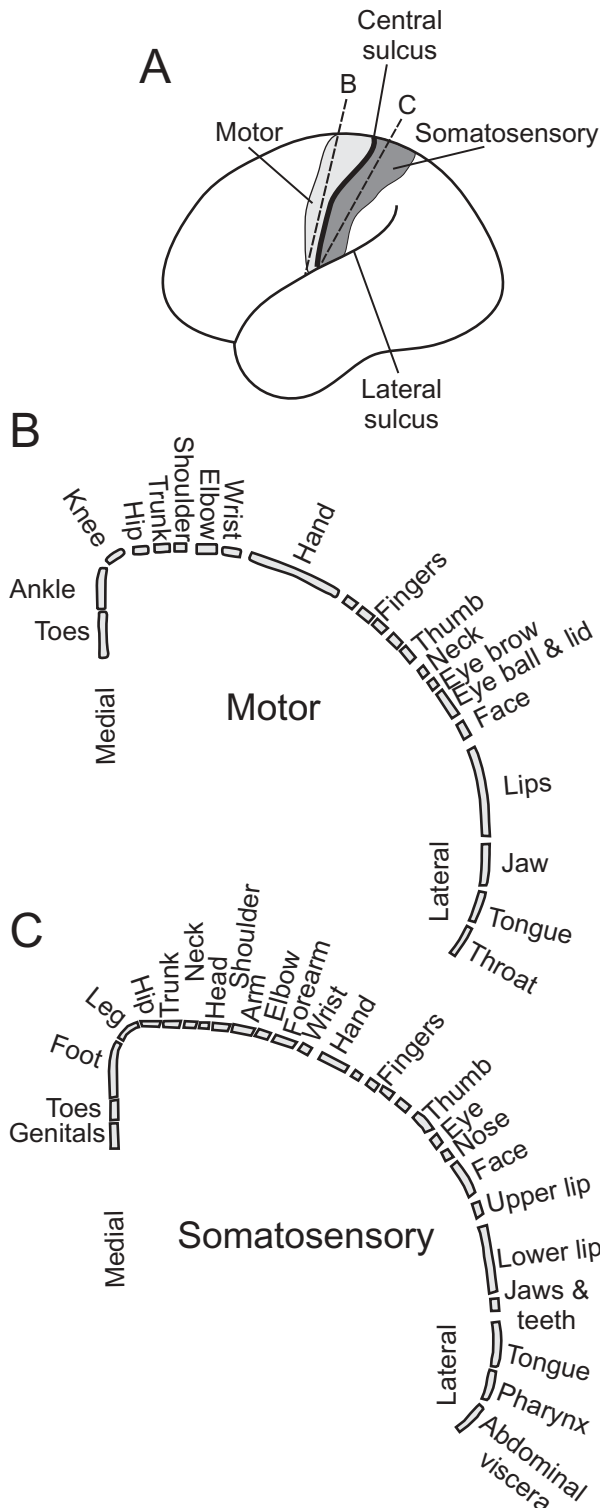


FIGURE 27-7. Examples of the variety of locations of somatosensory and motor cortices in five different mammals. Abbreviations: M, motor cortex; R, rostral area; PV, parietal ventral area; S, somatosensory cortex; S1, primary somatosensory map; S2, secondary somatosensory map; S + M, areas of overlap of somatosensory and motor cortices. Many mammals have more than one somatosensory map. Boundaries are approximate.

FIGURE 27-6. A: somatotopic maps of somatosensory cortex and motor cortex in a primate brain. The somatosensory cortex and the motor cortex are located on opposite sides of the central sulcus, which is indicated by a heavy line. The maps begin on the medial surface and continue onto the lateral surface. The maps are arranged with the caudal body parts represented most medially and the rostral parts represented ventrally and laterally. The broken lines on each map represent the planes of section shown in parts B and C. B: representation of a transverse section through the motor cortex along the plane shown in A. C: representation of a transverse section through the somatosensory cortex along the plane shown in A. In both B and C, the caudal body parts are located on the medial surface at the left. The hands, face, lips, jaws and tongue are located on the lateral surface curling down towards the lateral sulcus. Adapted from Kandel et al. (2001) and used with permission of Mc-Graw Hill.

cortex being in the motor area. In contrast to their fellow monotreme the platypus, echidnas have a somatosensory cortex caudal to and separate from their motor cortex. Unlike the situation in platypus, these areas do not overlap in echidnas. Among the North American marsupials, such as the American opossum, complete overlap is the normal condition, whereas in Australian marsupials, such as the brush-tailed possum, wombats, and wallabies, the situation is similar to that found in platypus, that is, partial overlap of the maps of the somatosensory and motor cortices occurs. Another example of this pattern may be seen in hedgehogs. In contrast to these, other mammals such as tree shrews, some rodents, some primates, and carnivores have a strip of cortex that separates the somatosensory map from the motor map.

The somatotopic maps of both the somatosensory cortex and motor cortex are laid out in roughly the same manner, with the most caudal structures being represented most medially, sometimes spreading over onto the medial surface of the hemisphere. The mid-body structures are located on the lateral surface, and the most rostral structures have their representation in the ventrolateral part of the somatosensory and motor cortical areas. Taste and vestibular sensitivity are represented here as well. The most ventrolateral representations in the somatosensory map are those of the viscera of the abdomen and thorax.

The point of this survey is to illustrate that considerable variability has been reported within and between various groups of mammals in the degree of separation of the somatosensory and motor cortices. This body of data must be regarded with some caution, however, as the distinction between sensory and motor areas can be a difficult one to make. Depending on the stimulus parameters, movements can be evoked from somatosensory cortical areas, and motor cortical areas can respond to somatosensory stimulation. The degree to which various groups of mammals actually vary in the organization of their somatosensory-motor cortices and the amount of overlap of the various areas need to be reevaluated in further studies.

A dramatic example of somatotopic organization may be seen in the duck-billed platypus, which uses its bill to feel about in muddy waters for food by use of both mechanoreception and electroreception; it has an enormous area of somatosensory cortex dedicated to these sensations from the bill. Figure 27-8(A) shows the distribution of these receptor types on the bill of a platypus. The areas of mechanoreceptors are shown in dark gray and the regions in which the electroreceptors are located are shown as light gray stripes. Figure 27-8(B) shows a map of the somatosensory areas. Note that S1 exists as two separate fields: 1) a ventrally-lying S1 region for the bill that contains areas responsive only to mechanoreceptors and other areas responsive to both mechanoreceptors and electroreceptors and 2) a much smaller, more dorsal region (unlabeled in the figure) for the trunk, limbs, and feet. Additional somatosensory representations are also present, each with representations of both the bill (dark gray shading) and the body. The bill portion of the **rostral area** represents mechanoreceptors and deep receptors, while the bill portion of the **parietal ventral area** represents only mechanoreceptors. The remaining areas of cortex are devoted to visual, audi-

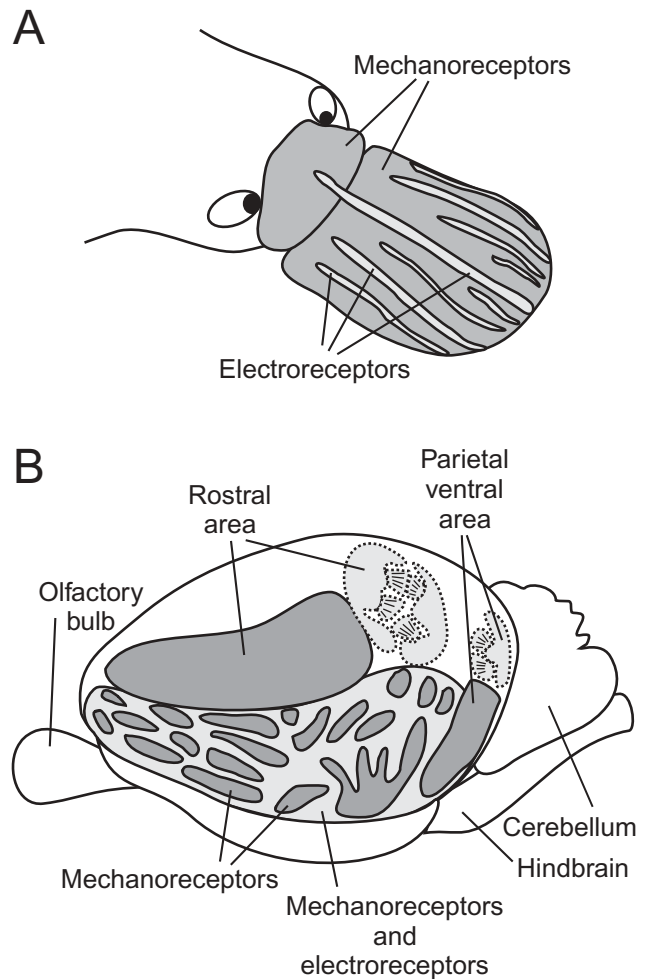


FIGURE 27-8. A: receptor types on the bill of a platypus. Areas of mechanoreceptors are shown in dark gray; regions in which the electroreceptors are located are shown as light gray stripes. B: somatosensory area S1 of a platypus, which exists as two separate fields: an S1 region for the bill, with mechanoreceptors and electroreceptors, and a separate, much smaller S1 field for the trunk, limbs, and feet (unlabeled). Additional somatosensory representations are also present: a rostral area and a parietal ventral area. See text for additional details. Adapted from Krubitzer (2000) and used with permission of John Wiley & Sons.

tory, and association areas. The motor cortex overlaps a portion of the somatosensory cortex.

Somatosensory Barrels. Another example of somatosensory mapping is the punctate representation in the **barrel fields** of the face areas of somatosensory cortex that receive input from the vibrissae (whiskers) in some mammals, including rodents and some marsupials. Because the vibrissae extend beyond the width of the face, they serve as a tactile early warning system; that is, they indicate that the face is about to touch something just before the contact is made. This information is extremely useful to animals that move about in

tunnels or narrow burrows or that squeeze their way through narrow apertures. Nocturnal animals also find the extensions of the face's tactile surface to be helpful in feeling their way through dark or dimly lit environments. What makes somatosensory representation of the vibrissae so extraordinary is that each whisker has its own dedicated cortical area. Because of the cylindrical shape of these cortical areas through the depth of cortical layer IV, they are known as **barrels**. Thus, each whisker has its own barrel. Moreover, the layout of the barrels in the cortical map is virtually a picture of the arrangement of the whiskers on the face. Figure 27-9 shows the vibrissae on the snout of a small rodent and its corresponding cortical barrel field. Note that while carnivores have well-developed vibrissae, they have not evolved the barrel specialization.

Somatotopic Organization Throughout the Somatosensory System. In addition to the somatotopic maps on the neocortex, somatotopic maps exist at all other levels of the somatosensory system as shown in Figure 27-10, which shows the representations of the fleshy, finger-like projections or "rays" from the snout of the star-nosed mole (see Fig. 1D and Fig. 2 in Box 2-3). Figure 27-10 shows the representation of the 11 nasal rays at the level of the principal nucleus of the trigeminal nerve in the hindbrain and in the VPM nucleus of the thalamus. An interesting feature of this particular specimen is the presence of an extra nasal ray, indicated in gray in the figure. Occasionally, a star-nosed mole is born with one or two additional rays or sometimes with one or two fewer. In all of these instances, the somatotopic map is a faithful representation of the receptor surface.

This type of representation throughout the system also occurs for the barrels. In the ventroposterior medial nucleus of the dorsal thalamus, there are correspondingly mapped regions called **barreloids**; likewise, in the principal sensory nucleus of the trigeminal, the vibrissae representations are in similar regions called **barrelettes**.

Multiple Representations of the Sensory Somatotopic Map. The somatosensory cortex has multiple representations in a number of mammalian species. In the visual system, the lem-

nothalamic visual nucleus predominantly projects to one visual representation, striate cortex, which is thus considered to be the visual lemnocortex, while the collothamic visual nucleus predominantly projects to multiple extrastriate visual representations that thus constitute the visual collocortex. In the somatosensory system, at least two representations, S1 and S2, receive projections from the somatosensory lemnothalamic nuclei. Additional representations may be present as well. The posterior insular cortex, which receives projections from the somatosensory collothamic nuclei, is considered to constitute the somatosensory collocortex.

Figure 27-11 is an illustration of a star-nosed mole somatosensory cortex from the same specimen shown in Figure 27-10. The heavy dotted line indicates the boundary between S1 and S2. As is often the case with multiple representations, the two somatosensory maps of the nasal rays are mirror images of one another, including the representation of the extra ray, shown in gray.

Traditionally, in anthropoid primates and prosimians, area S1 has been regarded as comprising Brodmann's areas 3a, 3b, 1, and 2. Because each of these areas contains a separate somatotopic map of the body, S1 is now considered to be coextensive only with area 3b. Preliminary evidence suggests that, in anthropoids and prosimians, both area 3a and area 3b are lemnopallial areas, whereas areas 1 and 2 are collopallial areas.

S2 usually is located ventral to S1. A full map of the contralateral body half exists in each of these areas. Usually the maps are mirror images of one another, that is, nose to nose. Typically, the S2 map is smaller and less detailed than the S1 map. Moreover, the S2 maps tend to have larger receptive fields than the S1 maps. This is the arrangement that has been described for rats and mice, eulipotyphlans (formerly called "insectivores"), and bats. In addition to the S1 and S2 maps, multiple representations of certain body parts that the animal uses extensively, such as vibrissae or hands, may have a second representation within S1. Three complete somatotopic representations have been found in the cortex of monotremes, and, among marsupials, opossums also have three complete representations. Other marsupials, such as wallabies and wombats, lack the dual representation of the vibrissae but do have a dual

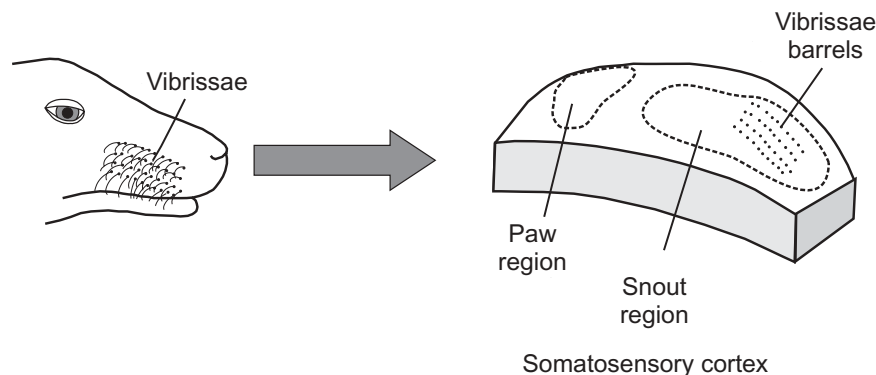


FIGURE 27-9. The somatotopic representation of the snout region of a rodent. Each vibrissa on the snout has its own representation as a "barrel" in the snout region of the map. The topographic distribution of vibrissae on the snout is the same as in the barrel field of the somatosensory cortex.

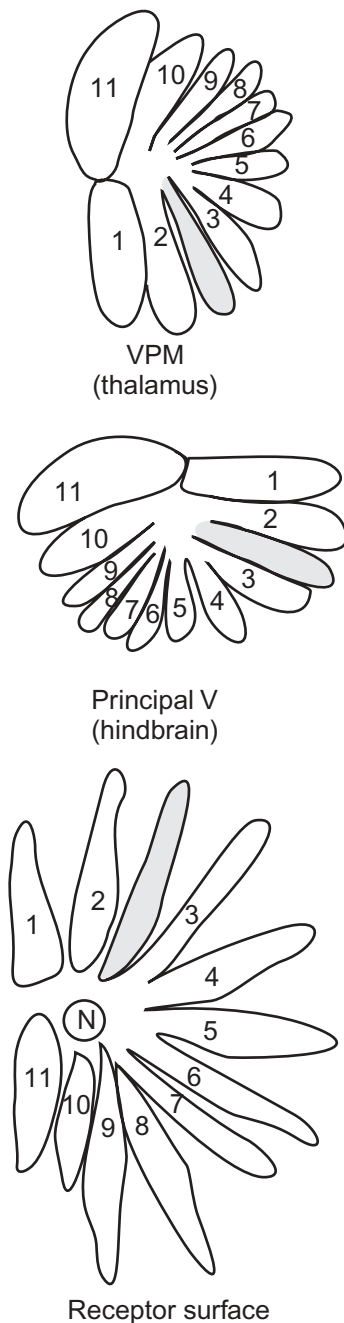


FIGURE 27-10. The receptor surface of the snout region of a star-nosed mole (bottom) showing the normal complement of 11 nasal “rays” plus an anomalous 12th ray, shown in gray. Middle: somatosensory organization of the snout region in the principal nucleus of the trigeminal nerve. Top: somatosensory organization of the snout region in the VPM nucleus of the thalamus. Note the presence of the anomalous ray in the middle and top maps. Adapted from Kaas (2000) and used with permission of John Wiley & Sons.

representation of the hairy skin of the upper lip. Some prosimians have a dual representation of the glabrous skin of the hand within S1. A similar dual representation of the forepaw has been reported in squirrels. Raccoons, which also make extensive use of the forepaw, have only a single representation of

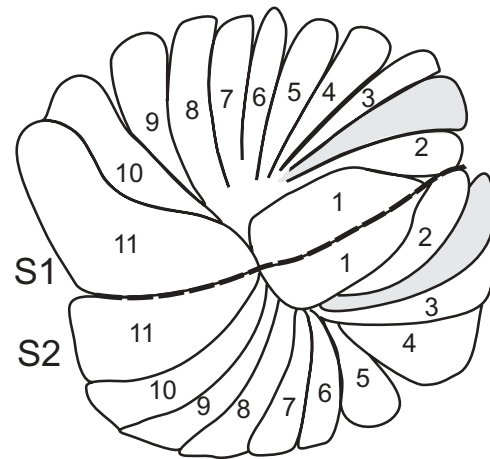


FIGURE 27-11. S1 and S2 of the neocortex of the same star-nosed mole as shown in Figure 27-10. The dotted line represents the boundary between these two areas. Note the presence of the anomalous ray in both S1 and S2. Adapted from Kaas (2000) and used with permission of John Wiley & Sons.

the glabrous forepaw, but it is enormous in size and contains many highly specialized subregions as well as very small receptive fields. In addition, representations of the hairy part of the forepaw are present as well.

Other species of mammals that have more than two somatosensory cortical areas, including the three somatosensory maps, are the tenrec (*Echinops telfairi*), a eulipotyphlan from Madagascar, and squirrels. Cats have not only S1 and S2, but an S3, S4, and S5 as well. Five somatosensory maps also have been observed in the North American opossum, a marsupial. Current thinking about the origin of multiple somatosensory maps is that at least two or three may have been a feature of the earliest mammals.

Old World and New World monkeys, in addition to having an S2 map, have two complete maps of the contralateral body half within the central strip of S1. In addition, on either side of the dual contralateral maps is a pair of matching maps that represent deeper tissues (such as muscles and joints) of the same body parts as in the central maps. Although these four maps are not completely identical to each other, the degree of correspondence between them is striking. Additional regions of somatotopic representation are the **retroinsular** (in back of the insula) cortex in primates, which may correspond to S4 in cats, and certain areas of the insula, the **granular** and **dysgranular insular areas**, which appear to be similar to S2, but rather more specialized for the face and hand. Finally, the **posterior parietal cortex**, which is located caudal to the somatosensory cortex and comprises Brodmann’s areas 5 and 7, receives its inputs from S1 (especially Brodmann’s area 2) and sends its efferents to S2.

Motor Cortex

The motor cortex has played a key role in experimental support for the concept that different biological and behavioral functions are localized in specific regions of the brain and, specifically, in the idea of topographic organization within the

brain. This support initially came from studies of damage to the motor cortex (usually war injuries and animal experiments) and electrical stimulation studies of patients during surgery. Studies that related small loci of damage in the motor cortex to localized regions of paralysis of body parts revealed the somatotopic motor map. These studies, in addition to the stimulation experiments, led to the view that voluntary movement is controlled by the motor cortex.

Multiple Motor Representations of the Body

Like its somatosensory counterpart, the cortical component of the motor system also has multiple body representations. For example, in some primates, up to six motor areas are present, each of which has a representation of the body. The **primary motor area**, which has been designated as **M1**, can be divided into rostral and caudal subdivisions; it is located in Brodmann's area 4, as shown in Figure 27-12, which is a monkey brain. Other motor areas, also shown in this figure, include a **supplementary motor area**, **M2**, and **dorsal and ventral premotor areas**. An additional premotor area has been reported on the medial surface of the cerebral hemisphere in the cingulate gyrus. This region corresponds to Brodmann's area 24. Because of its connections to other cortical motor areas, spinal cord, and motor thalamus, as well as electrophysiological criteria, the dorsal portion of area 24, known as area 24c, which is located within the depths of the cingulate sulcus, has been proposed as **M3**. Its connections with limbic cortex suggest that it may serve as one of the routes by which the limbic system can influence voluntary motor behavior.

If each of these areas contains a more or less complete representation of the body, how can we tell them apart? The answer is that the supplementary motor and premotor cortical areas are distinguished from primary motor cortex, and from each other, by the types of movements elicited by stimulation within each map, the complexity of the movements, and the amount of stimulation required to produce a movement.

The Cortical Eye Fields

Ventral to areas 4 and 6 is area 8. Parts of area 8 and the surrounding tissue constitute an area known as the **frontal eye field**. Stimulation of this cortical field results in strong movements of the eyes to the opposite side of the body. This area is regarded as containing command neurons for voluntary movements of the eyes and probably plays a role in the coordination of voluntary eye movements as well. The efferents of this area are to the oculomotor complex of the midbrain and the pontine reticular formation. The location of the frontal eye field may be seen in Figure 27-12.

An additional eye field is located in the occipital lobe, within the visual cortical areas, especially in V1 (striate cortex). This field is called the **occipital eye field**. In contrast to the frontal eye field, however, this region subserves involuntary eye movements of the sort that would result from the eyes pursuing some moving object in the visual field. The efferents of the occipital eye field are to the midbrain tectum.

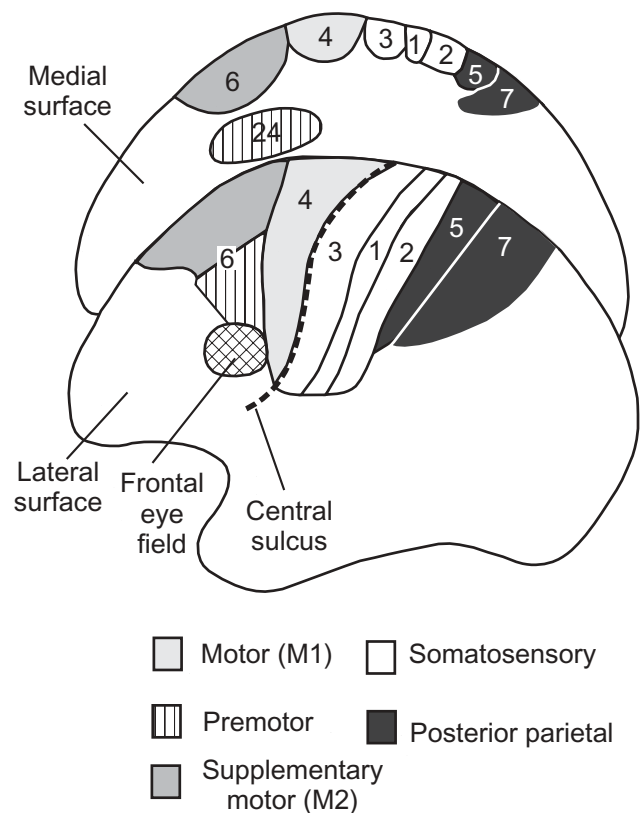


FIGURE 27-12. The location of some of the somatosensory and motor cortical areas of a monkey. The numbers refer to Brodmann's cortical areas. The primary motor cortex (M1) corresponds to area 4. The supplementary motor area (M2) is located in the dorsal and medial regions of area 6. The ventral region of area 6 and area 24 on the medial surface are known as premotor areas. A portion of area 24 contains an M3 region. Areas 5 and 7 constitute the posterior parietal motor-related areas. Also shown is the somatosensory area, which comprises areas 3, 1, and 2.

Afferents and Efferents of the Motor Cortex

The motor areas of the neocortex receive much of their input from the motor nuclei of the thalamus: VPLo, VL, and nucleus X, as shown in Figure 27-13. In addition to some afferents from S1, M1 receives most of its input from VPLo and VL, which are major conduits from the cerebellum and the striatum. M2 receives much of its input from VL, and the premotor cortex is supplied with afferents from nucleus X. M1, M2, and the premotor cortex are interconnected by a system of reciprocal connections.

As may be seen in Figure 27-14, which is based largely on studies of monkeys, the principal efferent pathway from the motor cortex is the **corticospinal tract** (or **pyramidal tract**) from motor cortex to the contralateral spinal cord. This pathway, which originates in M1, contributes approximately 50% of the corticospinal axons in primates. M1 is involved in voluntary movements of the body. Also included with these efferents is the **corticobulbar tract**, which controls voluntary movement of the face, head, and neck (see Chapter 12). The

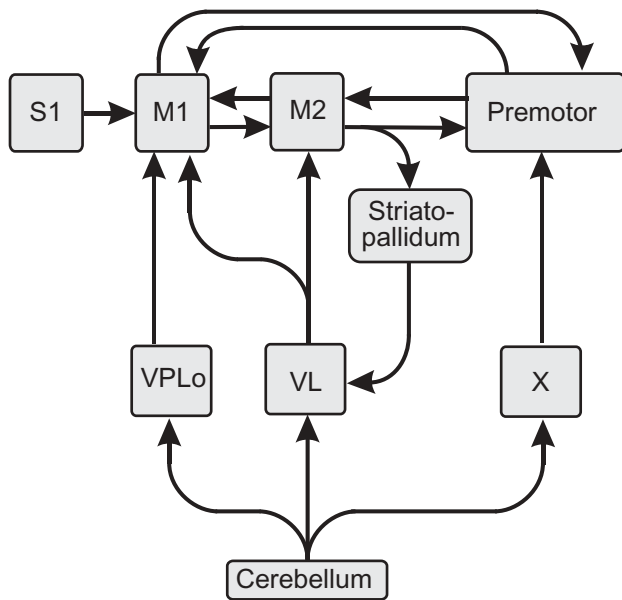


FIGURE 27-13. Schematic representation of the afferent pathways to cortical motor areas M1, M2, and the premotor areas. The inputs to these three cortical areas are mainly from VPLo, VL, and nucleus X of the ventral tier of the dorsal thalamus, from S1, and from one another. Abbreviations: VL, nucleus ventralis lateralis; VPLo, nucleus ventralis posterolateralis pars oralis.

pathway also participates in a feedback loop to the motor cortex via the pontine nuclei, the cerebellum, and motor thalamus. The remainder of the axons forming the corticospinal tract is from M2, the premotor area, S1, and areas 5 and 7 of the posterior parietal cortex.

Other efferents of motor cortex are to VPLo, VL, and nucleus X. M2 also participates in a feedback loop via the striatopallidum and VL. Thus, the motor thalamus is the crossroads of interaction between major somatic motor components: the motor cortex, striatopallidum, and cerebellum.

In many mammals, including many primates, rodents, and some carnivores (cats and raccoons), the corticospinal tract extends to the sacral level of the spinal cord. Only in humans, chimpanzees, and some monkeys, does the tract extend the entire length of the spinal cord to the coccygeal level. In other mammals, such as ungulates, rabbits, hedgehogs, and aardvarks, this tract reaches only as far as the cervical level. In other species, such as the spiny anteater, marsupials, tree shrews, some eulipotyphlans (moles), anteaters, and elephants, the corticospinal tract only penetrates the spinal cord as far as the thoracic region. Finally, in various carnivores, including dogs, and also in bats, and various rodents, the tract descends to the sacral level. Table 27-1 summarizes the depth of penetration of the corticospinal tract in a number of species of mammals.

The Corticobulbar Tract and Bagley's Bundle. Motor cortex control of the motor nuclei of the cranial nerves is carried out by axons of the **corticobulbar tract**, which originates in the face region of M1 and terminates directly on motor nuclei of the cranial nerves, such as motor V, motor VII, XI, and nucleus

ambiguus in primates. In nonprimates, the terminations of the corticobulbar axons are in the reticular formation cell columns adjacent to these motor nuclei.

In a number of ungulate species, the North American opossum, and possibly other mammals as well, a separate corticobulbar tract, known as **Bagley's bundle**, originates in the region of motor cortex that controls head and face movements in addition to the areas that control limb movement and terminates in the spinal nucleus of the trigeminal nerve and adjacent reticular formation (see Fig. 27-15). What distinguishes this pathway from the typical corticobulbar pathway is its ipsilateral termination pattern; most typical corticobulbar terminations are either bilateral or contralateral.

THE SOMATOSENSORY AND MOTOR FOREBRAIN OF NONMAMMALIAN AMNIOTES

The somatosensory and motor representations in the forebrains of reptiles and birds are much more limited than in mammals. The elaborate and highly detailed somatic and motor topographic maps of mammals are not a feature of the dorsal pallium in the telencephalons of the brains of reptiles, although some topographic maps of the body and face region have been reported in birds. Likewise, multiple representations of the body map, so typical of mammals, have not been reported in reptiles, although a report of such mapping in birds recently has appeared. The absence of such reports may be more a function of the extreme paucity of electrophysiological mapping studies in these animals, in comparison with mammals, than a definitive indication that somatotopically organized pallial maps do not exist. Similarly, there are few reports of pathways for direct dorsal pallial control of brainstem and spinal motor neurons. Major control of motor functions by the telencephalon seems to be a function of the striatopallidum (see Chapters 19 and 24) by way of brainstem coordinating systems such as the reticular formation and optic tectum (see Chapters 13 and 18).

Somatosensory System

The organization of ascending pathways via the dorsal thalamus in birds and reptiles follows a rather similar pattern to the somatosensory system of mammals. As in mammals, both collothalamic and lemnothalamic somatosensory pathways are present, as they are in the visual system. In addition, in reptiles, a lemnothalamic pathway from the trigeminal nuclei of the pons, which innervates the face and head, is juxtaposed to the lemnothalamic pathway from the body at both the dorsal thalamic and telencephalic levels. In birds, however, the trigeminal input bypasses the dorsal thalamus and terminates in a basal region of the telencephalic pallium that is specialized for somatosensory information from the beak, mouth, and face region; from there, a pathway proceeds to the somatosensory-motor region of the pallium.

Lemnothalamic Somatosensory System. Among nonmammalian amniotes, the lemnothalamic somatosensory system has

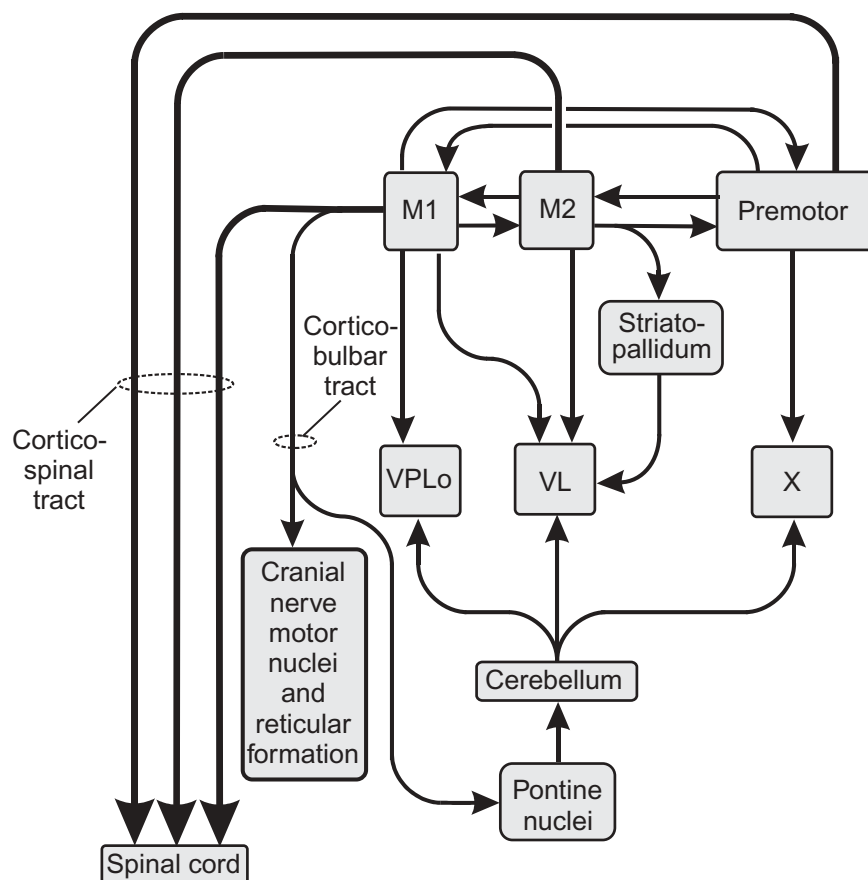


FIGURE 27-14. Schematic representation of the efferents of M1, M2, and the premotor cortical areas. The main efferents of the three motor cortical areas are to brainstem and spinal cord motor areas via the corticospinal and corticobulbar tracts, to pontine nuclei, which have connections with the cerebellum, and to the striatum. Abbreviations as in Figure 27-13.

Table 27-1. Maximum Depth of Termination of the Corticospinal Tract in Various Mammals. Adapted from Nieuwenhuys et al., 1998.

Spinal Cord Level of Termination	Species
cervical	goat, cow, deer, sheep, rabbit, hedgehog, aardvark
thoracic	phalanger, tree shrew, spiny anteater, elephant, wallaby, armadillo, mole, opossum
lumbar	bushbaby, lemur, kinkajou, dog, gopher
sacral	gibbon, loris, marmoset, some monkeys, raccoon, cat, chipmunk, bat, beaver, rat, hyrax, squirrel, hamster
coccygeal	chimpanzee, human, some monkeys

been most clearly elucidated in birds. The avian lemnothalamic pathway is very much like that in mammals. The ascending axons from the dorsal column nuclei in the caudal medulla terminate in a nucleus in the dorsal thalamus called **nucleus**

dorsalis intermedius ventralis anterior (DIVA). DIVA projects to a region of the rostral pallium, within the **hyperpallium apicale** (formerly known as the hyperstriatum accessorium), which is located anterior to the visual Wulst (the termination area of the visual lemnothalamic pathway) and could be considered therefore as a “somatosensory Wulst” (Figs. 27-16 and 27-17). Within this area is located the origin of a pathway similar to the pyramidal tract of mammals; thus, this region of the Wulst might better be termed a **somatosensory-motor Wulst**. Electrophysiological mapping of the somatosensory region of the Wulst indicates a somatotopic organization, with a highly precise map of the claw. In owls, two highly precise somatotopic representations of the skin of the claw recently have been found by Paul Manger, Guy Elston, and Jack Pettigrew.

Far less work on the somatosensory system has been done in reptiles than in birds. In lizards, a lemniscal somatosensory projection to part of **nucleus dorsolateralis anterior** in the dorsal thalamus and then to the dorsal cortex (Figs. 27-16 and 27-18) has been found. A recent study, however, indicates that this nucleus is polysensory, rather than exclusively somatosensory as is DIVA. In alligators, a rough topographic map of both the body and the head has been described.

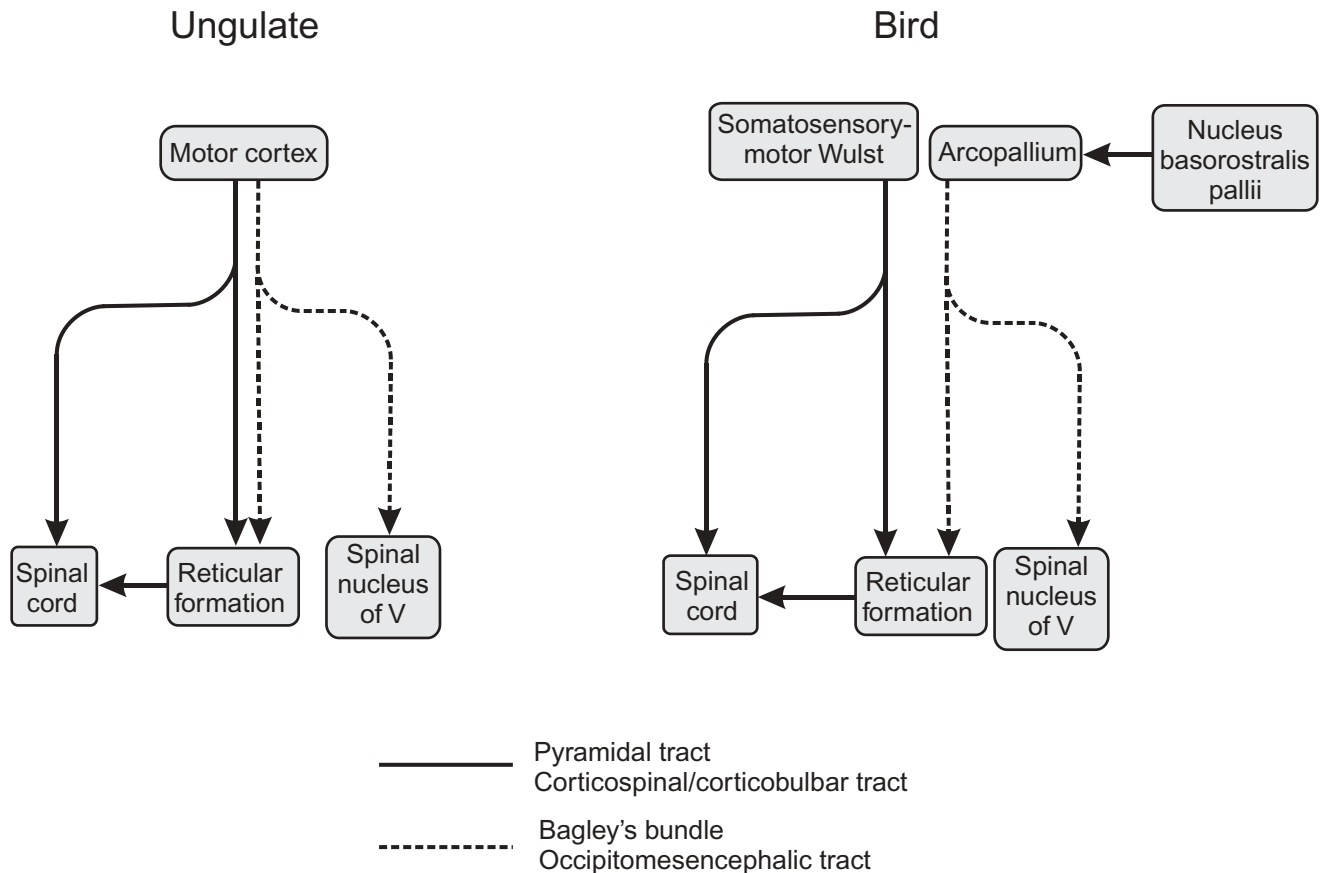


FIGURE 27-15. A comparison of the pyramidal tract and Bagley's bundle in an ungulate and the pyramidal tract and the occipitomesencephalic tract in a bird.

Sauropsid Trigeminal Pathways. The avian trigeminal pathway is not "thalamic" in the usual sense of the term because it has no thalamic component. The pathway, known as the **quintofrontal tract**, originates in the principal nucleus of the trigeminal in the pons and terminates in the basal, frontal telencephalon in a part of the nidopallium known as **nucleus basorostralis pallii** (Figs. 27-16 and 27-17), which was formerly called the nucleus basalis or nucleus trigeminalis telencephali. Why is this nuclear group in the telencephalon and not in the dorsal thalamus, like its mammalian counterpart, nucleus ventralis posteromedialis (VPM)? Some embryological evidence suggests that part of the ventrolateral complex of mammals originates in the telencephalon and eventually migrates to the diencephalon. If this is the case, then the basorostral pallial nucleus of birds may be the unmigrated homolog of VPM. Whatever the reason for its location, the pattern of efferents from this nucleus is what one would expect for telencephalic projections from a dorsal thalamic nucleus. Martin Wild, Fabiana Kubke, and Catherine Carr recently reported that the basorostral pallial nucleus contains somatotopic representations of the beak, face, and tongue as well as a tonotopically organized auditory region. The latter appears to be related to the auditory feedback from the action of the tongue and beak in vocalization. This topographical representation of the head and bill resembles the bill area of the platypus described above.

The efferents of the basorostral pallial nucleus are to two zones that also lie within the nidopallium of the anterior dorsal ventricular ridge. The first is directly dorsal to it and has been designated **nidopallium frontale, pars trigeminale**; the second projection field is in the caudal nidopallium and is known as **nidopallium caudale, pars trigeminale**. These two areas are reminiscent of the face and snout areas of S1 and S2 of mammals. This ascending trigeminal system has been implicated in the sensory control of pecking and grasping of food objects and the manipulation of them in the mouth to a point where they can be swallowed. Whether this avian trigeminal system is comparable to the lemnothalamic trigeminal pathway in reptiles and mammals is questionable due to the position of the basorostral pallial nucleus within the nidopallium as well as its receipt of ascending auditory input.

In lizards, ascending axons from both the principal nucleus of the trigeminal nerve and the descending nucleus of this nerve arrive at the somatosensory component of the thalamic nucleus dorsolateralis anterior, which is the same nucleus that receives the somatosensory representation of the body. The map of the face and snout, therefore, is coextensive with the map of the body, rather than being topologically separate as in birds and mammals. See Figure 27-18 for a summary of the ascending lemnothalamic somatosensory pathways of reptiles, shown with solid lines.

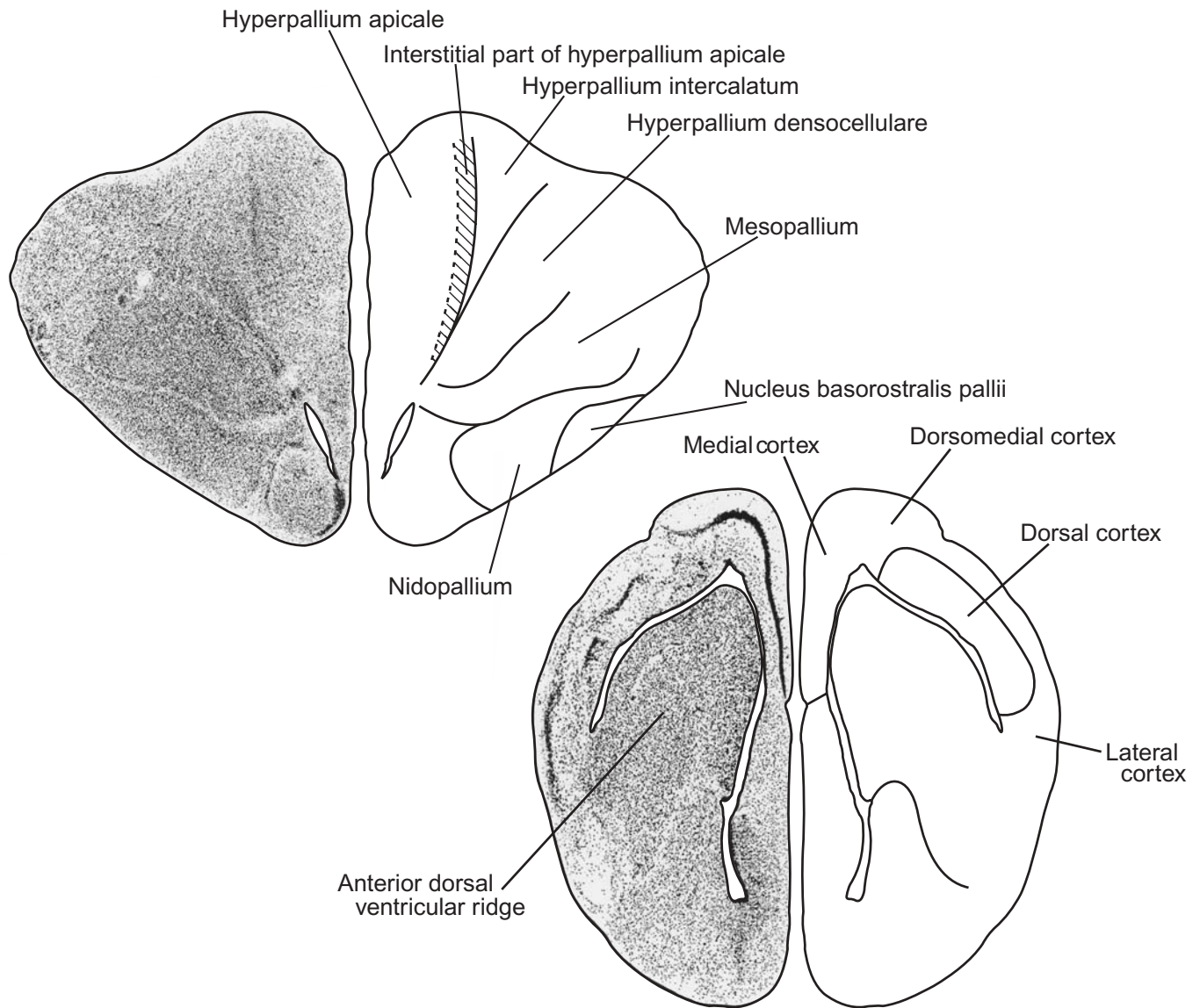


FIGURE 27-16. Transverse hemisection with mirror-image drawing through the somatosensory Wulst in the telencephalon of a bird (*Columba livia*) at top left. The area of termination of the somatosensory lemnothalamic projection is indicated by diagonal lines. Adapted from Karten and Hodoss (1967) with additional data from Wild (1987b). Used with permission of The Johns Hopkins University Press. Transverse hemisection with mirror-image drawing through the telencephalon of a lizard (*Tupinambis nigropunctatus*) is shown at bottom right. The location of the putative lemnothalamic telencephalic somatosensory area is within the dorsal cortex. Adapted from Ebesson and Voneida (1969) with the somatosensory area inferred from Bruce and Butler (1984a). Used with permission of S Karger AG, Basel.

Collothalamic Somatosensory System. In reptiles, ascending axons from the spinal cord and dorsal column nuclei ascend to the midbrain somatosensory area in the tectum. From the tectum, somatosensory projections ascend to terminate in the **medialis complex** in the dorsal thalamus. The medialis complex sends its efferents to a region of the anterior dorsal ventricular ridge that lies between the target region of projections from nucleus rotundus (the collothalamic visual counterpart to the medialis complex) and the target region of

axons from nucleus reuniens pars compacta, which is the auditory collothalamic nucleus that we will encounter in Chapter 28. Examples of the telencephalic termination field of the medialis complex are shown in a turtle in Figure 27-19 and in an iguana in Figure 27-20. This pathway in reptiles is summarized with broken lines in Figure 27-18.

The thalamic counterpart of the collothalamic somatosensory pathway in birds comprises two nuclear areas: **nucleus semilunaris parovoidalis** and the caudal part of **nucleus**

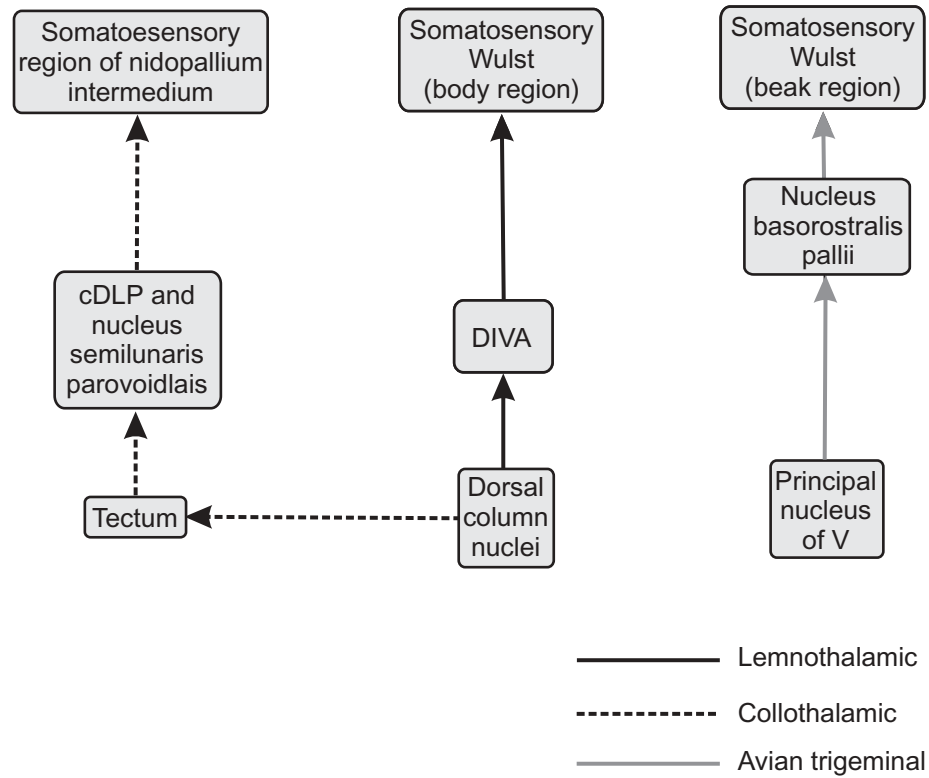


FIGURE 27-17. Somatosensory pathways in birds.

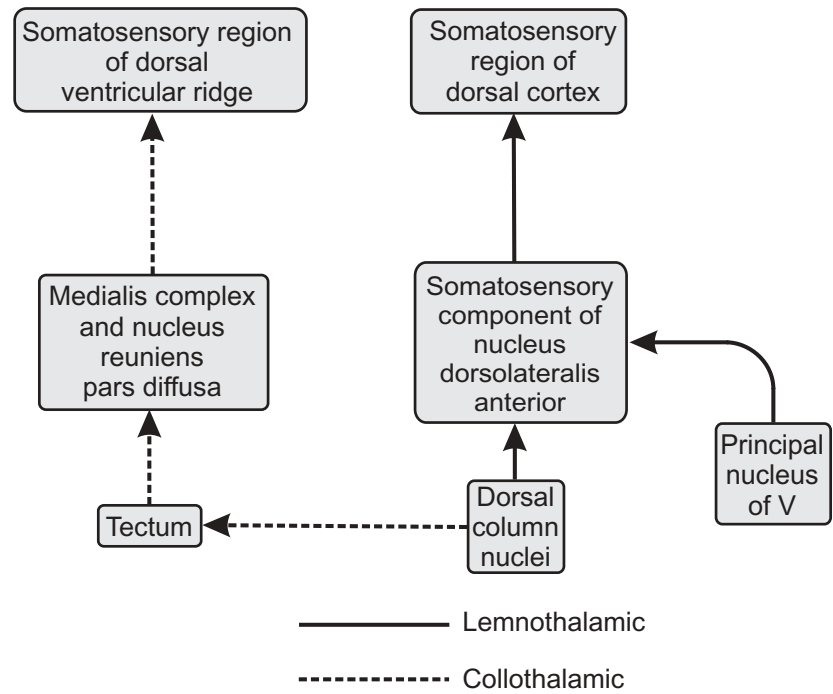


FIGURE 27-18. Somatosensory pathways in reptiles.

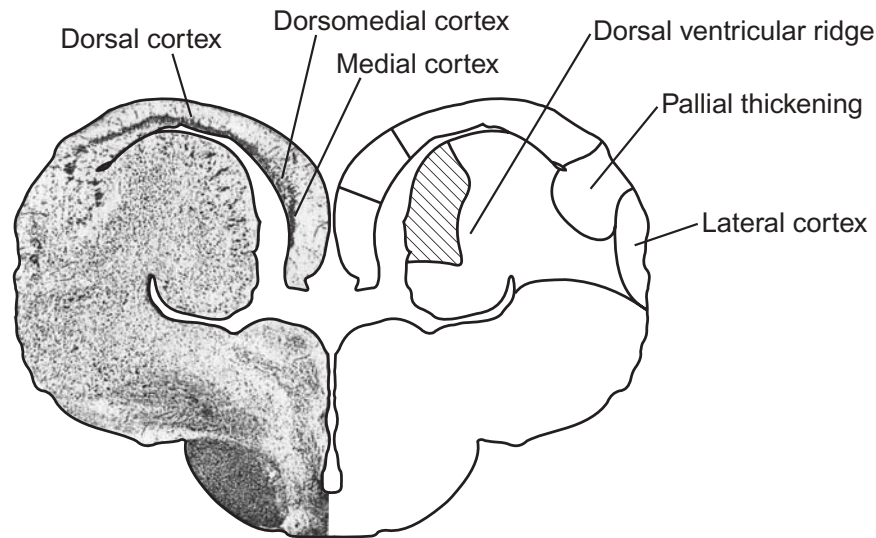


FIGURE 27-19. Transverse hemisection with mirror-image drawing through the telencephalon of a turtle. The location of the collothalamic telencephalic somatosensory area in the dorsal ventricular ridge is indicated by diagonal lines. Adapted from Balaban and Ulinski (1981) and used with permission of John Wiley & Sons.

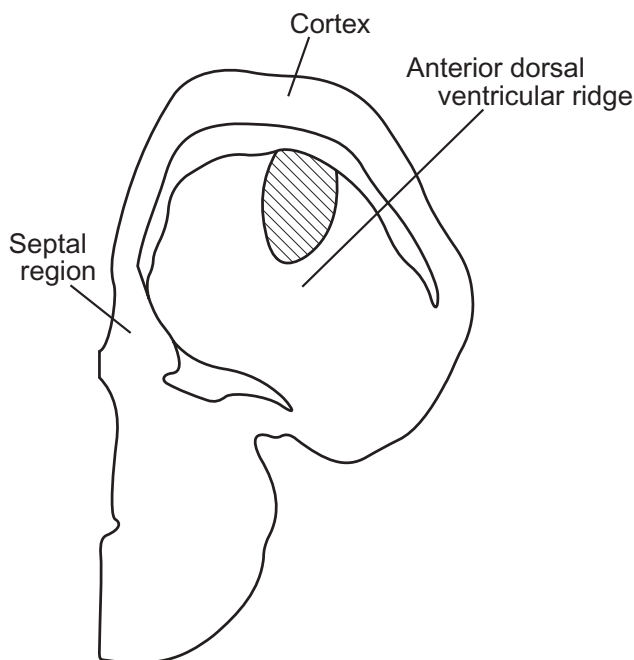


FIGURE 27-20. Drawing of a transverse hemisection through the telencephalon of a lizard (*Iguana iguana*). The location of the collothalamic telencephalic somatosensory area in the dorsal ventricular ridge is indicated by diagonal lines. Adapted from Bruce and Butler (1984b).

dorsolateralis posterior (cDLP). These nuclei send their efferent axons to the **nidopallium intermedium**, which is a region within the avian anterior dorsal ventricular ridge (Fig. 27-21). The rostral region of nucleus dorsolateralis posterior appears more closely related to the collothalamic visual system.

Motor System

The relatively limited somatosensory representation in the telencephalon in reptiles and birds may be related to the relative dearth of descending motor pathways from the telencephalon to central pattern generators associated with motor nuclei of the brainstem and the spinal cord. Neurons in a lateral part of the telencephalon of birds, called the **temporo-parieto-occipital area** (Fig. 27-21), may constitute a cortical-like motor area. Similarly, neurons in the medial-to-central part of the dorsal cortex in gecko lizards have been found to project to the striatum. Other descending pathways arise in regions that are sensory or are closely related to sensory structures. Because a pathway is descending does not guarantee that it is motor. Sensory systems may require descending pathways to the reticular formation for such behavioral functions as focusing attention on a particular sensory target, which may have little or nothing to do with motor function in the sense that motor cortex is related to movement in mammals.

Recent research has revealed that birds have a thalamo-telencephalic motor system that bears a number of resemblances to the comparable system in mammals. Martin Wild and Matthew Williams have reported a pathway in two species of finches that originates in the motor region of the somatosensory-motor Wulst and passes directly to the cervical spinal cord. This pathway bears a striking resemblance to the pyramidal tract of mammals. This region also sends axons to the reticular formation and the red nucleus, both of which project to the entire length of the spinal cord. The somatosensory-motor Wulst efferent pathway has additional terminations in the pontine nucleus and inferior olivary nucleus, both of which are part of a feedback loop to the cerebellum and thence to the red nucleus. Thus, the somatosensory-motor Wulst is able to influence motor neurons of the spinal cord via the direct pyramidal route and by way of the reticulospinal and rubrospinal tracts, at least, and possibly by way of the vestibulo-

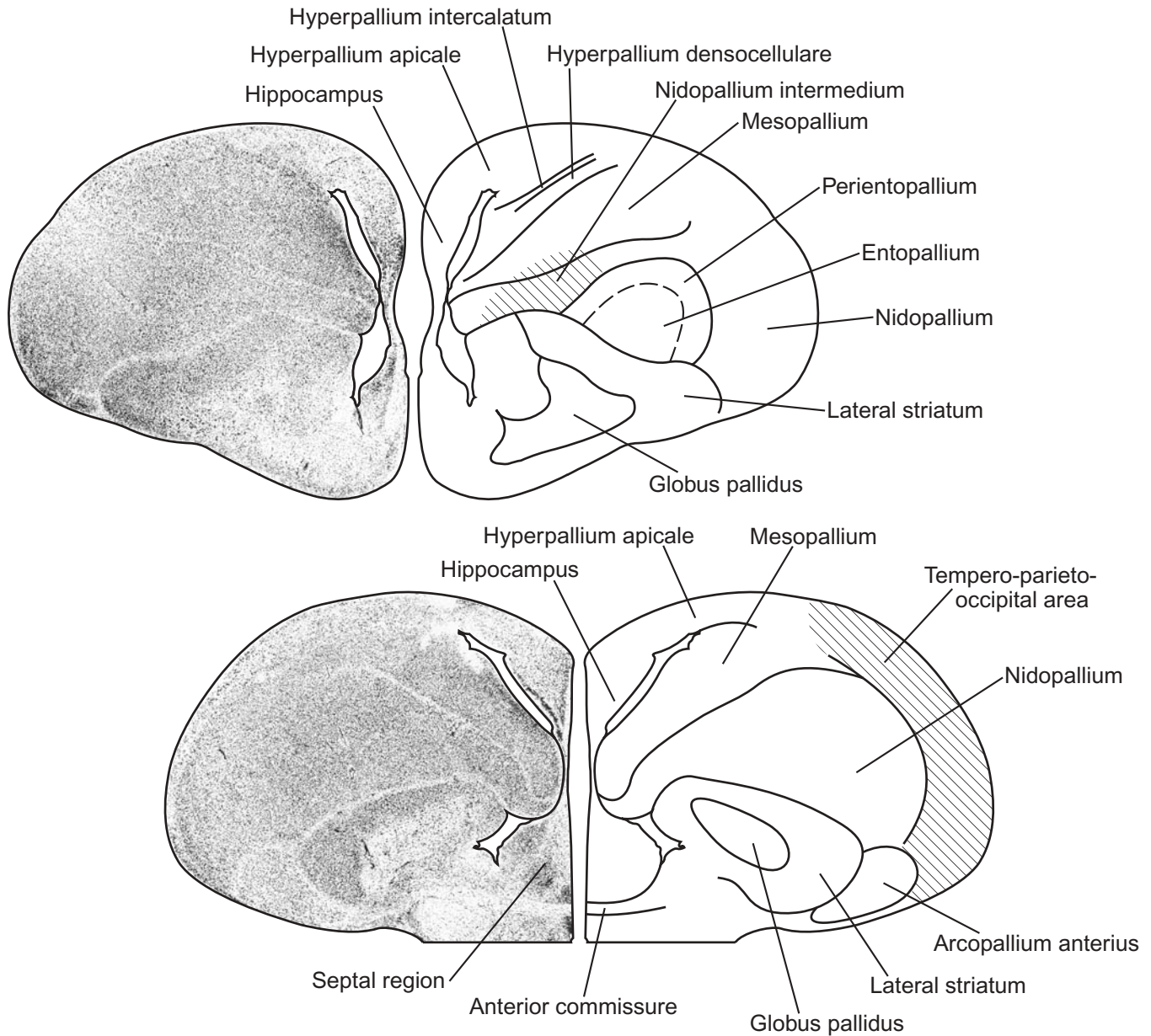


FIGURE 27-21. Transverse hemisections with mirror-image drawings through the telencephalon of a bird (*Columba livia*). The top section is the more rostral one. The location of the collothamic telencephalic somatosensory area in the nidopallium intermedium (formerly called the neostriatum intermedium), within the dorsal ventricular ridge, is indicated by the more medial area of diagonal lines. The location of the parieto-temporal-occipital area is indicated by the area of diagonal lines in the lateral part of the telencephalon. Adapted from Karten and Hodos (1967) with additional data from Wild (1987b) and Brauth et al. (1978). Used with permission of The Johns Hopkins University Press.

lospinal system via the cerebellum as well. Finally, Loreta Medina, Leo Veenman, and Anton Reiner make the case that the thalamic **ventrointermediate area (VIA)**, by virtue of its topographic position, its histochemistry, and its connections, is the avian equivalent of the motor thalamus (VA, VL, and VPLo) of mammals. Figure 27-22 is a schematic representation of the avian pyramidal motor system.

In addition to the pyramidal system, birds have a second descending motor pathway from the telencephalon. This pathway is related to the ascending pathway from the trigeminal system to the nucleus basorostralis pallii. Some of the efferents of the latter nucleus terminate in a region of the arcopallium, which in turn gives rise to descending projections. This descending pathway, the **occipitomesencephalic**

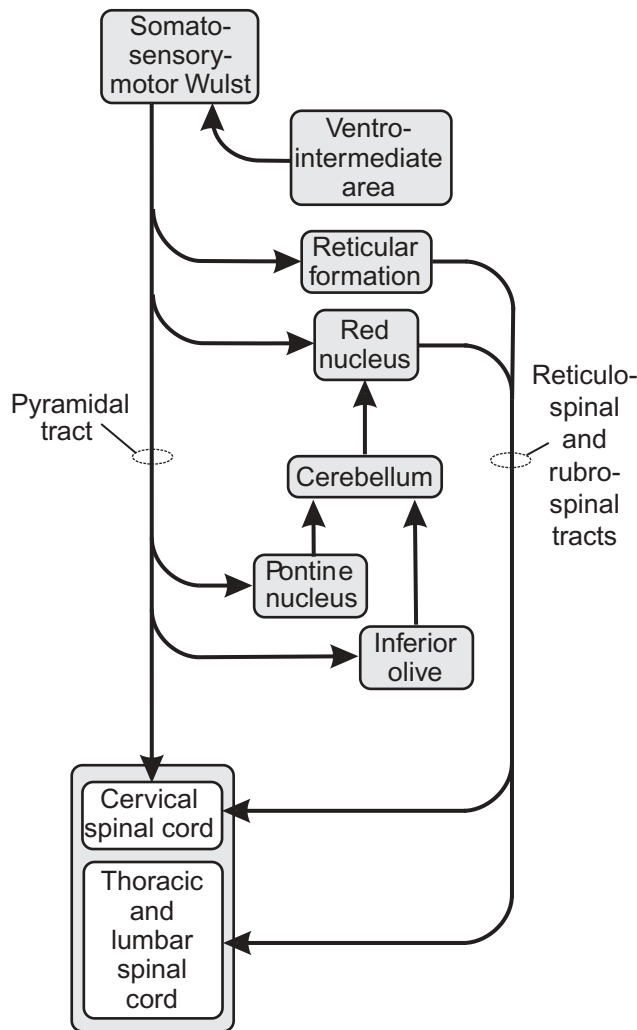


FIGURE 27-22. Motor pathways in birds.

tract, has a number of similarities in common with **Bagley's bundle** of ungulates. It terminates in the spinal nucleus of the trigeminal nerve and its adjacent reticular formation, both of which send projections to the spinal cord. A major difference between the occipitomesencephalic tract and Bagley's bundle is that the latter originates in the face region of motor cortex, whereas the occipitomesencephalic tract originates in a separate telencephalic region from the somatosensory-motor area. Figure 27-15 compares Bagley's bundle and the pyramidal (corticospinal and corticobulbar tracts) in an ungulate with the occipitomesencephalic tract and pyramidal tract in a bird.

As discussed in Chapter 24, birds have a dorsomedial thalamic zone that comprises several individual nuclei. These nuclei participate in circuits with the striatopallidum and the pallidum. They include **nuclei dorsomedialis (DM)**, **dorso-lateralis (DL)**, and **dorsointermedius posterior (DIP)**. Among their pallial targets is the nidopallium of the dorsal ventricular ridge, which in turn projects to the **arcopallium intermedium**. The latter is the source of a descending pathway to the reticular formation. Although the specific role of these nuclei in the avian motor system remains to be

elucidated, their circuitry suggests that they participate in the initiation and/or control of voluntary movements.

One of the main routes to the control of central pattern generators and motor neurons in reptiles is via the cerebellum and its connections to a variety of descending spinal pathways, such as the rubrospinal tract and the reticulospinal tract. An additional pathway, as in birds and to a much more minor degree in mammals, is via the striatopallidum to the tectum to influence the tectospinal pathway.

EVOLUTIONARY PERSPECTIVE

In contrast to the elaborate telencephalic somatosensory and motor systems of mammals, those of birds and reptiles are more modest. What factors might have led to the elaboration of these systems in mammals while leaving them relatively less developed in the other amniote groups? One possible factor might have been the evolution of hair as the mammalian skin covering. Because of the vastly greater numbers of hairs on mammalian skin than of scales on reptiles or feathers on birds, the skin has the capacity to be a much more sensitive receptor sheet in mammals than in the other amniote taxa. The increased number of hairs also allows for a heightened sensitivity to precisely where on the body surface some stimulation occurs and to how large is the area of contact. Where we see the presence of a sophisticated somatosensory surface in non-mammalian amniotes, such as the claw skin of an owl, a more mammal-like central organization occurs with detailed mapping of the sensory surface and multiple representations along the lines of the mammalian model.

A second consideration is the development in mammals of direct telencephalic control over premotor and motor nuclei of the spinal cord. Increased precision in the use of digits, especially in great apes, simian monkeys, raccoons, and rodents such as rats, squirrels, chipmunks, and hamsters, and to a lesser extent prosimians, dogs, tree shrews, eulipotyphlans, monotremes, and marsupials, has led to the development of the elaborate corticospinal motor system that is characteristic of mammals. Many reptiles and birds have the capacity to manipulate their digits and can perform prehensile motor acts in grasping objects such as tree limbs, seizing prey as do predatory birds, or manipulating their eggs or food objects. The digital abilities of these animals, however, are very limited in comparison with those of a squirrel, for example, deftly manipulating an acorn as he chews first on one side and then on the other, a monkey delicately lifting a tasty insect held between thumb and index finger to her mouth, or a human typing a manuscript. The latter precision motor behaviors require the collaboration of a sophisticated somatosensory system to provide the feedback necessary to permit the motor system to calibrate its commands precisely in accordance with the immediate consequences of those commands.

Finally, while the collothalamic ascending somatosensory system is a shared and relatively conservative feature across amniotes, interesting differences exist in the organization of the other ascending pathways. A lemnothalamic somatosensory pathway is also a common feature of amniotes, at least for the somatosensory innervation of the body, but birds and mammals may have evolved their discrete thalamic relay nuclei for this

system independently by a process of parcellation of the lemnothalamus, rather than possessing them as a heritage from their common amniote ancestors. The trigeminal system is more problematic, at least in birds. While reptiles and mammals share a clearly lemnothalamic, trigeminal pathway to the somatosensory pallium, birds lack a thalamic relay for their trigeminal system. Like lemnothalamic pathways, most of the trigeminal projections bypass the midbrain roof, but they terminate in what must be regarded as collopallial territory, i.e., within the basorostral pallial nucleus, a component of the nidopallium. The evolutionary history of this system remains to be illuminated.

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Auditory and Vocal Forebrain in Amniotes

INTRODUCTION

In this chapter, we will continue our discussion of sensory and motor aspects of the forebrain. This time, however, we will be discussing the world of sound and how its detection and production are organized in the dorsal thalamus and telencephalon and present a review of the relevant connections with the hindbrain.

Sound waves are a form of rhythmic disturbance of the surrounding medium. More specifically, they are longitudinal pressure waves that are generated by mechanically moving surfaces in an elastic medium. They also can be generated by vortices or turbulence in the medium. For animals that live in air, such as humans, this means that some disturbance of the environment produces a rhythmic pattern of movement of air molecules sufficient to cause the tympanic membrane (eardrum) to vibrate. This pattern of vibration is detected by the hair cells in the cochlea (see Chapter 2) and is transmitted to the brain. Some animals, like moles, move through tunnels of earth; the earth conducts vibrations to the air in the tunnel surrounding the animal where these vibrations are detected by its auditory system. For animals that live in water, the stimulus to be detected is a disturbance of the water molecules surrounding it.

In this chapter we also will describe the forebrain pathways that participate in the control of vocal production. Vocal productions (and their detection) are important in the lives of animals as social signals to identify individuals, to keep animals in contact with each other when they are out of sight, to establish and maintain territories, to attract mates, to warn of predators, and to threaten intruders. In some special cases, such as

owls, bats, and dolphins, hearing is used to detect the location of prey by accurately localizing the source of sounds in space. In the case of owls, the salient sounds are those made by the prey as it moves through the surrounding environment of leaves, grass, and twigs. Bats, however, use both the vocal and auditory systems to produce sounds that reflect off the prey (or other objects); these reflected signals are then detected by the bat. Bats can then “compute” the location in space from which the sounds were reflected. A similar vocal-auditory system is used by dolphins. Neuronal populations and pathways in the forebrain play a role in the production, detection, and interpretation of vocal signals and other sounds. Indeed no sound signal has any value unless it can be detected and interpreted.

In this chapter, we will make frequent reference to auditory structures and axonal pathways of the hindbrain and midbrain that were described in Chapters 11, 12, 15, and 17. The reader might want to briefly review these chapters before going further in this chapter.

Location of Sound Sources

The location of a sound source is one of the most important aspects of the acoustic world that an animal must process. In order to make an accurate determination of source location, an animal must make use of the differences in the signals that arrive at its two ears. If we had only one ear, we would have to turn 360° in order to determine the direction from which the sound seemed to be the loudest, which would be the direction of the source. Two ears, however, permit source direction to be determined without moving the head at all, although head movements can improve directional accuracy. The

acoustical stimuli that enter the two ears are known as **bin-aural** signals (bi = two, and aural = ear). The differences between the acoustical signals that reach each ear, because of their different locations in space, are called **binaural cues** to direction. These binaural cues are largest when the sound source is directly in line with the entrance to one of the two ears. Three types of binaural differences can occur when the source is lined up directly with the entrance to the ear, which are illustrated in Figure 28-1.

- **Binaural time difference** is the difference in time required for the sound wave to reach the second ear after arriving at the first ear. This difference is very short and is

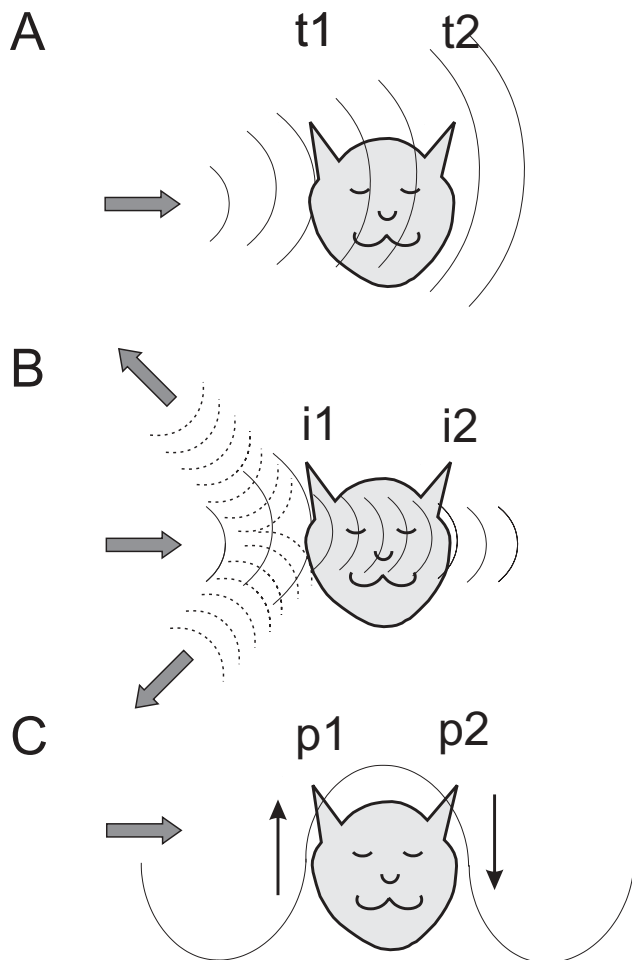


FIGURE 28-1. Binaural cues to the localization of sounds in space. The arrows indicate the direction of the sound wave. A: binaural time difference. The sound arrives at the near ear at time 1 (t_1), which is sooner than when it arrives at the far ear at time 2 (t_2). B: binaural intensity difference. Sound is reflected from the head on the near side so that the far ear is in the sound “shadow” of the head. Thus the intensity at the near ear (i_1) is greater than the intensity at the far ear (i_2). C: binaural phase difference. The near ear receives the rising phase of the sound wave (p_1) at the same instant that the far ear receives the falling phase (p_2). Binaural phase differences depend on the frequency of the sound wave and the spacing between the ears.

determined partly by the speed of sound (which can vary slightly in different atmospheric conditions) and partly by the size of the head (which determines the distance between the two ears). This time difference is less than 1 ms for humans and shorter for animals with smaller heads. Owls make exceptional use of this cue in their superb ability to detect the source of a sound made by a prey animal, such as a small rodent. Figure 28-1(A) shows the sound arriving at the near ear at time 1 (t_1) and later at the far ear at time 2 (t_2).

- **Binaural intensity difference** results from the second ear being in the sound “shadow” of the head. Just as the head can cast a shadow when a beam of light is shined on it, so it can cast a sound shadow to an acoustical wave because some of the sound is reflected off the first side of the head, which reduces intensity at the second ear, and some of the sound gets absorbed by the head, which further reduces the intensity at the second ear. Figure 28-1(B) shows some of the sound being reflected from the near side of the head, which makes the intensity at the near ear (i_1) greater than the intensity at the far ear (i_2).
- **Binaural phase difference** occurs when the acoustical wave that arrives at the first ear is out of phase with the wave arriving at the second ear; that is, the first ear may be receiving a rising phase of the wave at the same instant that the second ear is receiving a falling phase of the wave. The availability of this cue depends on the relationship between the distance between adjacent peaks of the acoustical wave, which is inversely proportional to their frequency, and the distance between the two ears. This binaural cue is of particular importance to small animals that have ears so close together that the time difference is too short for the nervous system to process. Likewise, their small heads do not produce enough of a shadow for a detectable binaural intensity difference. Since others of their own species (and occasionally potential predators) typically are the most frequent target of vocalizations, small animals have become adapted to vocalize in frequency ranges that maximize the effectiveness of the binaural phase-difference cues of their intended listeners. In Figure 28-1(C), the near ear receives the rising phase (p_1) of the sound wave at the same instant that the far ear receives the falling phase (p_2).

Echolocation

Many prey objects make virtually no sound as they move through their environment, such as a moth flying through the night sky. Others have the sounds that they make masked by other sounds from the environment, such as fishes swimming in the sea. Certain predators have overcome these disadvantages by producing vocalizations and listening for the echoes of these vocalizations as they are reflected off objects in the environment. The capabilities of these animals are so extraordinary that they can detect the size, shape, speed, direction, and even surface features of the objects that reflect back the acoustic waves of these vocal emissions. The two groups of animals that have become highly adapted for the skillful use of these mechanisms are the microchiropteran bats and dolphins.

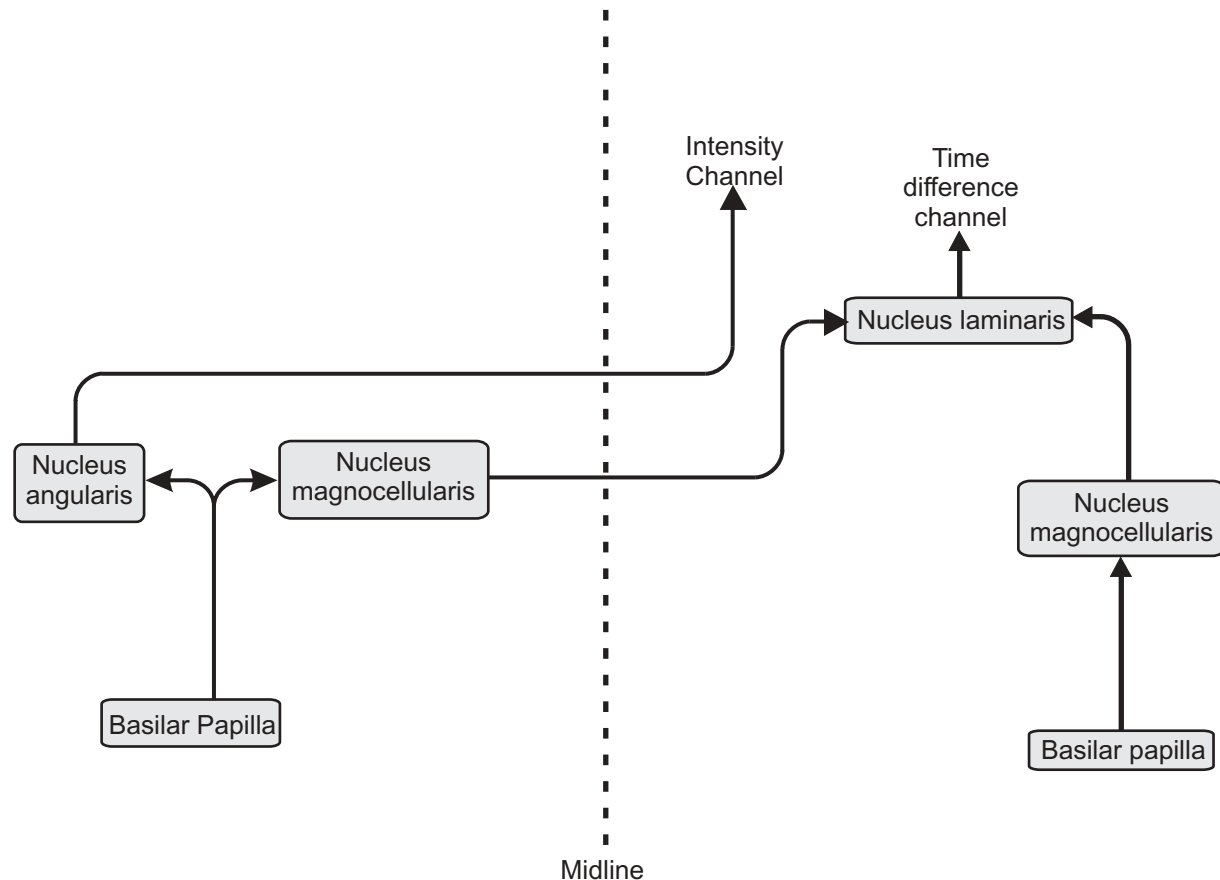


FIGURE 28-2. The cochlear nuclei and nucleus laminaris in an owl. Nucleus magnocellularis projects bilaterally to nucleus laminaris, shown here on the right side. Because of the differences in arrival time of the neural impulses from the two sides, a time-difference channel is established in this pathway leading to higher regions of the brain. These time differences represent different azimuths in acoustical space. The nucleus angularis codes intensity information. Information about the frequency of acoustical stimuli is coded in both channels. A comparable system exists on the left side of the brain.

Auditory Channels for Time and Intensity

To the extent that an animal uses the binaural time difference to localize the source of a sound, whether the prey is the primary source, as in the case of owls, or whether prey is reflecting an acoustical wave generated by the listener, as for bats and dolphins, the auditory system must be capable of detecting and processing minute time differences. Likewise, the phase and intensity differences must be processed as well. In some reptiles and birds, two nuclear groups in the hindbrain form a timing channel. These are the **nucleus magnocellularis**, which is one of the cochlear nuclei that receive the axons of the auditory nerve, and the **nucleus laminaris**, which is a target of the magnocellular nucleus. As shown in Figure 28-2, nucleus laminaris receives axons from both the ipsilateral and contralateral nucleus magnocellularis and computes the time difference between the signals at the two ears. It is able to do so because the action potentials (or spike potentials) of the auditory nerve are **phase locked**; that is, each action potential or spike is generated at the same phase of the acoustical wave. When the spikes tend to occur at approxi-

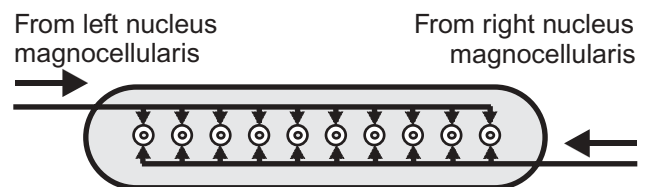


FIGURE 28-3. A schematic representation of the input from each nucleus magnocellularis to nucleus laminaris of an owl. The nucleus laminaris neurons act as coincidence detectors. This arrangement forms a delay line that corresponds to an azimuthal map of acoustical space. Nucleus laminaris is also shown in Figure 11-15.

mately the same location (also known as the “phase angle”) on each successive wave, they are said to be “phase locked.” The neurons in nucleus laminaris form an azimuth map (right to left positions) of auditory space based on arrival-time differences of phase-locked auditory action potentials.

Figure 28-3 shows a schematic drawing of nucleus laminaris in an owl in which an axon from the left nucleus mag-

nocellularis enters from the left end of the nucleus and in which an axon from the right nucleus magnocellularis enters from the right end. Each incoming axon gives off a collateral branch to a number of nucleus laminaris neurons. If the acoustic stimulus is coming from the animal's left, an action potential will arrive at the neuron at the extreme right end of the nucleus via the last collateral of the axon at the same time that an action potential arrives via the first collateral coming from the right side because of the time delay required to reach the more distant right ear. This arrangement is known as a **delay line**. The neurons of nucleus laminaris, in turn, act as **coincidence detectors** by responding only to simultaneous stimulation from the right and left sides. The particular neuron that responds represents the point in space that is the source of the sound. In owls, the nucleus laminaris is very well developed compared with this nucleus in birds such as chickens that do not have the superior localization capabilities of owls. Mammals lack a nucleus laminaris. On the other hand, their **medial superior olivary nucleus** of the hindbrain performs the phase-locked encoding of binaural time differences and may be homologous to the nucleus laminaris of nonmammalian amniotes.

In addition to time and phase, the auditory nerve in birds also provides information about intensity. This latter information is processed in the other cochlear nucleus, **nucleus angularis**, which is the origin of the intensity channel. Figure 28-2 also shows nucleus angularis as the origin of the intensity channel. Frequency is coded in both the nucleus angularis and the nucleus magnocellularis and the subsequent nuclei of the auditory pathway. Most authorities regard the ventral and dorsal cochlear nuclei of mammals as homologues of the avian nuclei angularis and magnocellularis, respectively, which process the corresponding components of the auditory input.

This brief discussion of the coding of binaural differences and the central representation of auditory space is intended only to give the reader a flavor of the structure-function relationships that exist in the auditory system. A fuller treatment of this rich topic may be found in the references to review articles and research reports at the end of this chapter.

DESIGN FEATURES OF THE AUDITORY SYSTEM

Topographic Organization

Topographic organization of sensory systems has been a major theme of Chapters 26 and 27 on vision and somesthesia and the motor system. In this chapter, we will encounter this mapping principle again but in a form quite different from before. In the topographic maps that we have already discussed, the topography that was mapped was of space, either the visual space around the animal or the spatial map of the body. In the case of the auditory system, the topography is one of frequency, time delay, and other parameters of the sound waves that make up the acoustical signals to be detected. Thus, the maps that we find in the auditory system represent the physical properties of sound waves that are laid out in an orderly, systematic fashion, such as high tones at one end of the map, low tones at the other end, and intermediate tones

located in the middle. A topographic organization based on the frequencies of tones is known as a **tonotopic organization**. Similar orderly maps can be found for other acoustic parameters depending on the particular property of the sound that the animal must process, such as the location in space of the sound source, or its speed and direction, if it is a moving source. Tonotopic organization can be found at each level of the auditory pathway from the peripheral auditory organs to the telencephalon.

Bilateral Interaction in the Auditory Pathway

Another important design feature of the auditory system that makes it different from the visual or somatosensory systems is the rich network of interconnections between the right and left auditory pathways at each level. In general, the visual and somesthetic pathways of the right and left sides are kept separated until the telencephalon, where the right and left topographic representations can interact via commissural axons. In contrast, commissural axons are present at every level of the auditory system from the pons and medulla, where the auditory axons of the cochlear branch of cranial nerve VIII enter and go through their initial stages of processing, through to the telencephalon. The only exception is at the level of the auditory thalamus, which appears to lack any commissural connections. The high degree of bilateral interaction probably has been selected for due to the importance of making constant comparisons of the signals at the two ears for the crucial information about directionality. This constant comparison of stimuli on the right and left is not a feature of somesthesia, and the closest counterpart in vision would be the comparison of stimulation of corresponding points on the two retinas that is the basis of stereoscopic vision.

Descending Auditory Pathways

In addition to ascending pathways, another design feature of the auditory system is the presence of descending pathways from the auditory forebrain to the auditory midbrain and hindbrain auditory nuclei. The **superior olivary nucleus** or, if several olivary nuclei are present, **the superior olivary complex**, is a major hindbrain target of these descending pathways. It is the source of the **efferent cochlear pathway** or **olivocochlear bundle**. This pathway terminates on the hair cells of the cochlea or equivalent auditory organ in the inner ear. This efferent pathway affects membrane potentials in hair cells and thereby can have a variety of effects on the functions of the cochlea such as selective tuning for specific acoustic frequencies.

AUDITORY PATHWAYS IN TETRAPODS

In Chapters 26 and 27, the discussion of the visual, somatosensory, and somatomotor pathways was limited to amniotes because of the relative paucity of data on these systems in anamniotes. Anamniote pathways and neuronal groups were discussed where appropriate in earlier chapters

on the hindbrain, midbrain, and forebrain. A considerable amount of work has been done, however, on both the auditory and vocal control pathways of anuran amphibians; we deemed it appropriate to include them in this chapter for ease of comparison with amniotes.

In the two preceding chapters, we saw that the somatosensory system and the visual system each have both collothamic and lemnothalamic pathways to the telencephalon. The auditory system, however, only has collothamic pathways to the telencephalon; that is, all ascending routes to the dorsal thalamus are via the auditory midbrain. It is possible that the vestibular system comprises the lemnothalamic moiety for the eighth cranial nerve.

Anurans. Figure 28-4 is a representation of the ascending pathways from the hindbrain to the telencephalon in two frogs; Figure 28-4(A) is of several species from the genus *Rana*, and

Figure 28-4(B) is of *Xenopus laevis*, an aquatic frog that retains both gills and a lateral line system into adulthood. The latter has recently been studied in detail by Christofer Edwards and Darcy Kelley. In anurans, the ascending auditory pathways from the hindbrain (the **dorsal medullary nucleus**, the **superior olivary nucleus**, and the **nucleus of the lateral lemniscus**) terminate in the torus semicircularis of the midbrain. In *Rana*, all three nuclei of the torus, the **magnocellular nucleus**, the **laminar nucleus**, and the **principle nucleus**, receive bidirectional projections from the hindbrain, but of the three only the principal nucleus is organized tonotopically. In *Xenopus*, only the laminar nucleus receives the projections from the hindbrain. The toral nuclei in *Rana* in turn project to three thalamic nuclei: the **anterior nucleus**, the **central nucleus**, and the **posterior nucleus**. Projections to the telencephalon include a pathway from the anterior nucleus that projects to the medial pallium and one from the central nucleus

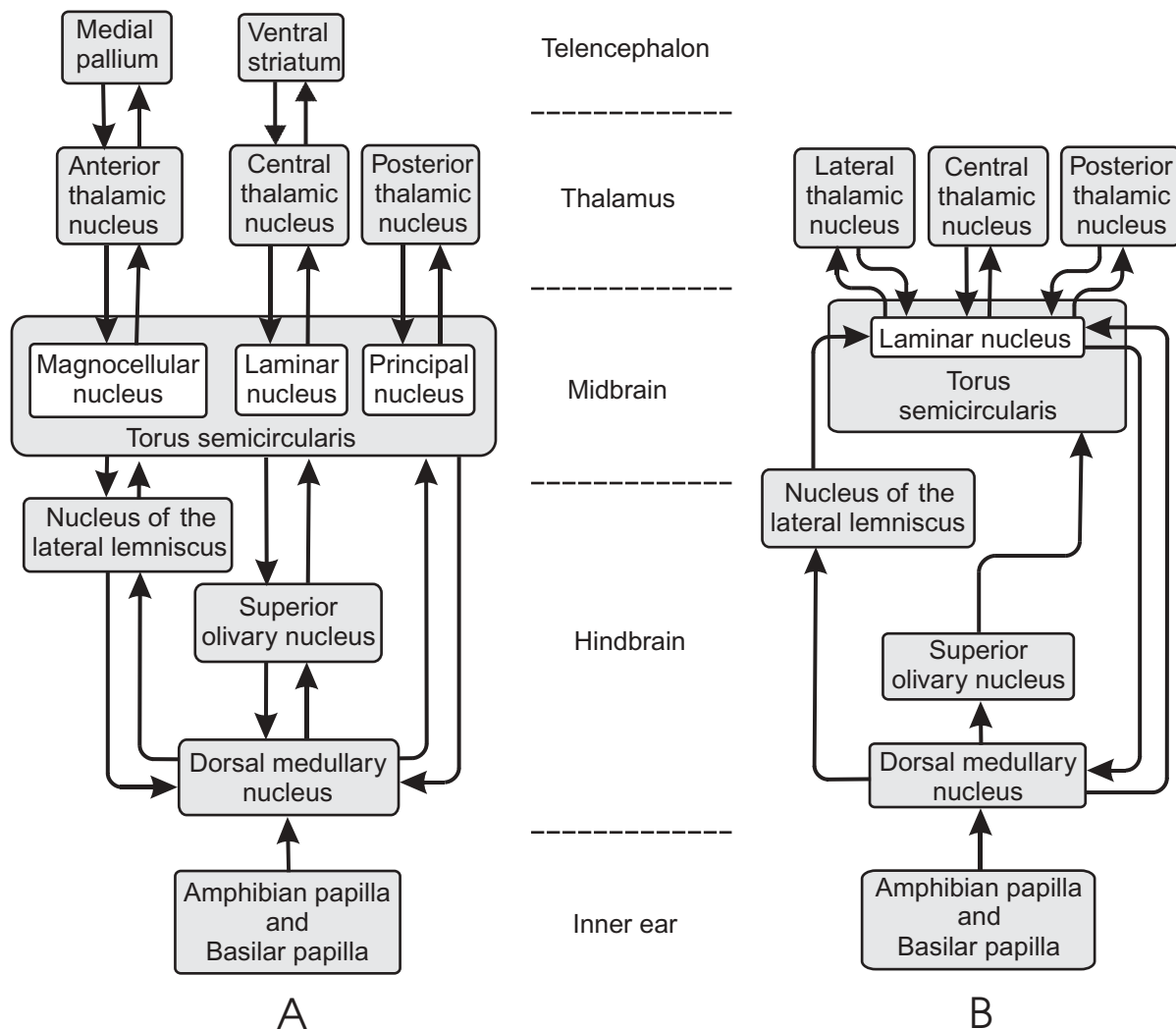


FIGURE 28-4. The major auditory pathways of frogs. A: a ranid frog. All three nuclei of the torus semicircularis are connected by bidirectional projections to the auditory nuclei of the hindbrain. The efferent connections of the individual toral nuclei are to different thalamic targets. B: *Xenopus laevis* based on Edwards and Kelley (2001).

that terminates in the ventral striatum. No telencephalic projections from the thalamus have as yet been reported in *Xenopus*.

Birds. The main thalamic auditory nucleus in birds is **nucleus ovoidalis**, so called because of its ovoid shape. It receives the ascending auditory pathway from the auditory midbrain. Nucleus ovoidalis projects to the auditory **area L pallii** (formerly known as Field L) of the telencephalon in the dorsal ventricular ridge. Area L pallii will be discussed in greater detail later in this chapter. Figure 28-5 shows the avian auditory pathways from the hindbrain to the telencephalon. Note the separate pathways for intensity and time difference channels and that these channels ascend together to the mesencephalon in the lateral lemniscus.

Reptiles. The general organization of the auditory pathways in reptiles has many similarities in common with the corresponding pathways in birds. Lizards, crocodiles, and snakes have a single thalamic auditory nucleus, **nucleus medialis**, that is equivalent to the avian nucleus ovoidalis. In crocodiles and turtles, this same nucleus is known as **nucleus reuniens**, which means the “reuniting” nucleus, because in crocodiles the two nuclei on either side are fused across the midline. In crocodiles, the nucleus reuniens has two divisions: **nucleus**

reuniens, pars compacta and **nucleus reuniens, pars diffusa**. Both divisions of nucleus reuniens receive ascending axons from the auditory midbrain, but the more substantial termination field is within the compact division. The central division relays auditory input to a discrete part of the dorsal ventricular ridge.

Mammals. The mammalian thalamic auditory nucleus is called **nucleus geniculatus medialis**, or **medial geniculate nucleus**, or often **medial geniculate body**. The medial geniculate nucleus has several subdivisions that vary both with species and the names assigned to them. In general, however, three main subdivisions, sometimes with additional subunits, seem to be the most common description. These three subdivisions are **medial**, **ventral**, and **magnocellular**. The magnocellular division of the medial geniculate nucleus should not be confused with the magnocellular cochlear nucleus, which is located in the hindbrain and receives axons of the cochlear branch of nerve VIII. Figure 28-6 presents a schematic diagram of the ascending auditory pathways in mammals. Note the similarity in overall organization to the avian pathways in Figure 28-5 and in particular that all of these pathways shown in Figures 28-4 to 28-6 terminate in the auditory midbrain before continuing on to the thalamus and telencephalon.

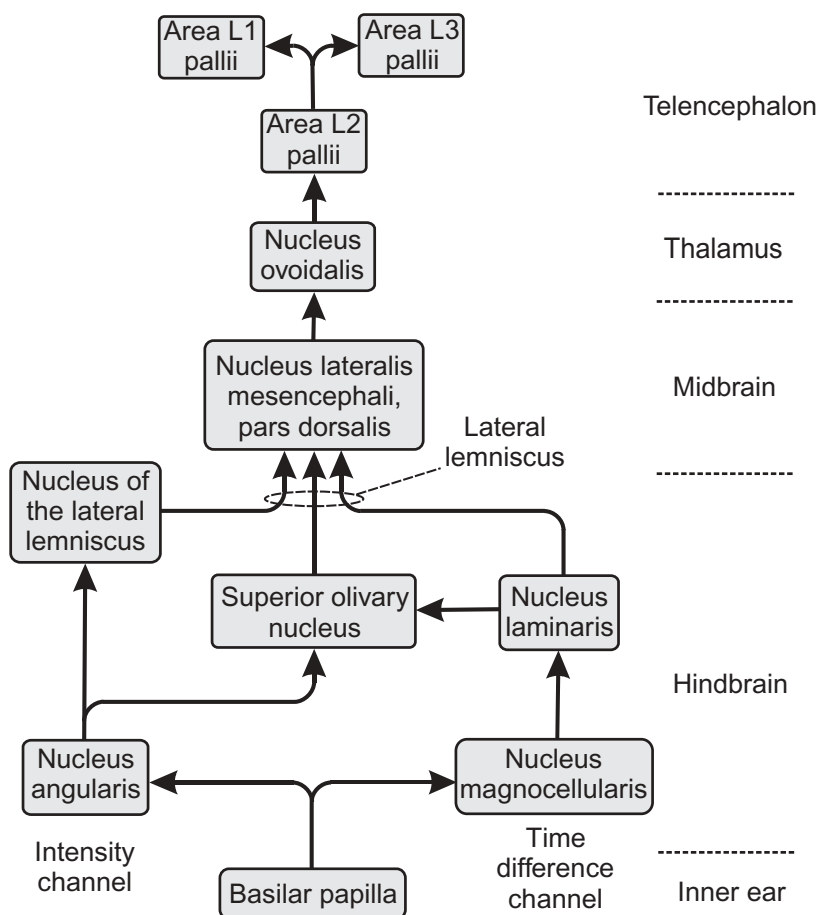


FIGURE 28-5. The major auditory pathways of a bird.

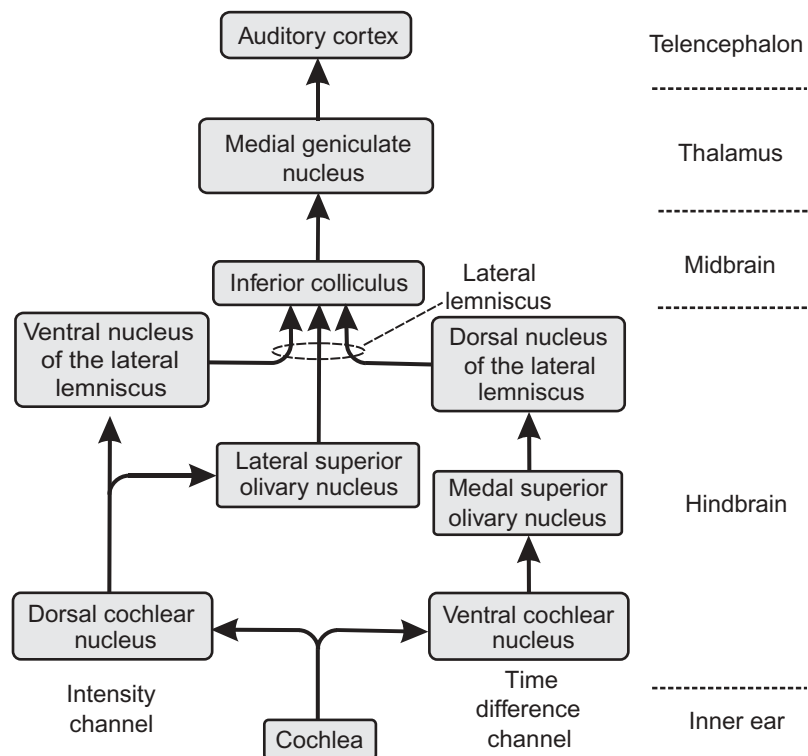


FIGURE 28-6. The major auditory pathways of a mammal.

We will take this opportunity to remind you of a point made in Chapter 26, namely, that the medial geniculate nucleus (or body) is not the auditory equivalent of the dorsal lateral geniculate nucleus (or body) of the visual system because the medial geniculate nucleus is collothalamal and the lateral geniculate nucleus is lemnothalamal. With this caveat having been noted, we must now mention that the ventral division of the medial geniculate nucleus nevertheless has certain features in common with the pars dorsalis of the lateral geniculate nucleus; that is, it has a laminar organization with a tonotopic organization within each lamina.

AUDITORY TELENCEPHALON

Columnar Organization

Like the visual and somatosensory cortices that we discussed in the two preceding chapters, the mammalian auditory cortex also has a columnar organization. The avian auditory telencephalon, which has been the most intensively studied among the nonmammalian amniotes, also has a columnar organization with different acoustical frequency bands of the tonotopic organization being represented as vertical columns through the individual laminae that are the structural organization of this area. In mammals, an additional type of organization, similar to the hypercolumns of visual cortex, has been described, which consists of alternating pairs of horizontal bands through the cortex. The neurons in one band of the pair are excited when both ears are stimulated; the neurons in the adjacent band are excited when one ear is stimulated but are

inhibited when the other ear is also stimulated. These auditory “hypercolumns” (reminiscent of the visual hypercolumns described in Chapter 26) provide the telencephalic representation of auditory space. Figure 28-7 shows a schematic representation of tonotopic and columnar organization in a mammal. Figure 28-14 shows tonotopic and columnar organization in the equivalent avian area, known as area L pallii.

Mammals

A feature of the visual, somatosensory, and motor cortices is multiple representation of either the spatial body map or the map of visual space. Mammals also have multiple representations of the auditory map, but it is a tonotopic map, not a representation of auditory space. The main tonotopic map is referred to as area **A1**. In the Brodmann nomenclature of human cortical areas, the primary auditory cortex is found in areas 41 and 42, which are located on the medial surface of the temporal lobe and into the depths of the lateral sulcus. The region containing the secondary map is designated as area **A2**. A1 and A2 typically exist as a pair, with the sequence of tones in A1 and A2 reversed so that the high-frequency end of A1 is adjacent to the high-frequency end of A2. In addition, a number of other tonotopic maps have been found in different species of mammals. Differences both in organization and nomenclature make comparisons difficult. In general, however, these additional areas form a semicircular or circular **auditory belt** around A1 and A2. Marsupials appear to have only a primary or A1 area. Most eutherian mammals examined thus far have at least A1 and A2. In addition, other cortical areas in which the

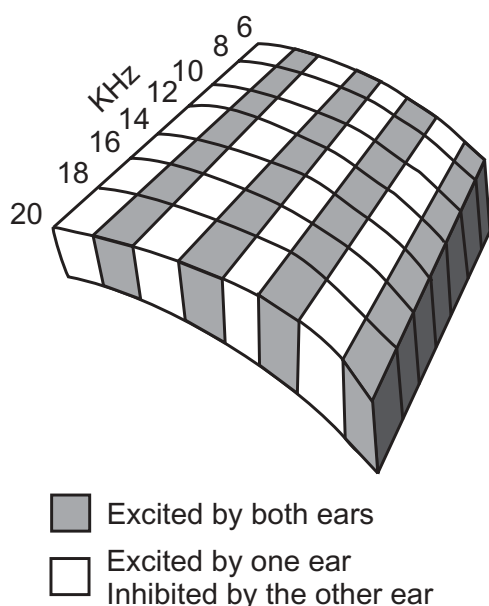


FIGURE 28-7. Columnar and tonotopic organization in the auditory cortex of a cat. The tonotopic organization is the orderly representation of acoustical frequencies. Adjacent pairs of horizontal columns are excited by acoustical stimulation of both ears or are inhibited by stimulation of one ear and are excited by stimulation of the other. These pairs of columns are similar in some respects to the hypercolumns of the visual cortex.

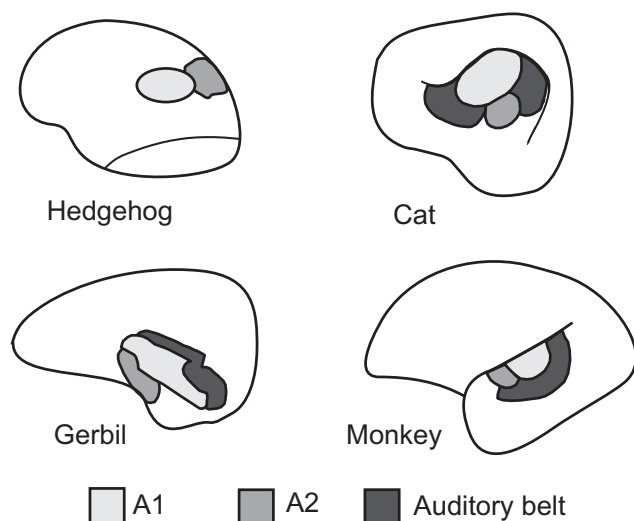


FIGURE 28-8. The major subdivisions of the auditory cortex in four mammals.

neurons respond to acoustical stimuli have been reported, but these are not tonotopically organized. In Figure 28-8, we present examples of the auditory cortex in several mammalian species with their individual tonotopically organized regions indicated. For simplicity of discussion, however, we will refer to three regions: A1, A2, and the auditory belt.

Bats. The microchiropteran bats are nocturnal and make use of echolocation to identify prey and other objects, including their distance, speed, and direction of movement. Their auditory cortex is organized in a highly complex manner. Because bats are moving through space as they emit their high-frequency vocalizations, the speed of the movement of the bat is added to the speed of the acoustical wave as it leaves the bat and is subtracted from the speed of the returning echo signal as it bounces off a stationary object. This is the **Doppler shift** phenomenon that affects the pitch of sounds. A common example of the Doppler shift can be observed in the increase of pitch in the siren of an emergency vehicle as it approaches you and then a decrease in its pitch as it passes and moves away from you. As it passes you, the pitch of its sound drops as the speed of the vehicle is first added to the speed of the sound wave and then subtracted from it. Bats must compensate for the Doppler shift in order to make accurate distance, speed, and direction estimates. In addition, the reflections from a moving target, such as a fluttering moth, are much more complex than those from a stationary tree and produce complex Doppler shifts in the frequencies of the returning echoes. Bats can make not only these compensations, but they can use the Doppler-shift information to identify different types of insects. These abilities are represented in the organization of their auditory cortex.

Figure 28-9 shows a schematic representation of some of the many specialized areas of the auditory cortex of a mustache bat that have been described by Nabuo Suga and co-workers. The diagram shows a large tonotopic map that extends well into the ultrasonic range with a very large area of cortex dedicated to the 61-kHz frequency, which is the frequency of the animal's echolocation vocalization. This animal also has a number of additional areas that respond either to constant-frequency stimuli or to stimuli in which the frequency is rapidly changed (frequency-modulated stimuli). These correspond to the types of acoustical signals that are reflected from various surfaces in its environment including its prey. By taking advantage of differences in the amplitudes, delays, Doppler shifts, and other characteristics of these reflected signals, the bat can make extremely accurate estimates of the size, distance, velocity, azimuth, elevation, and even fine details of the surfaces that reflect its vocalizations. The auditory systems of bats have been the subject of intense investigation, and this brief description does not do justice to the rich detail and the amazingly sophisticated organization that has been elucidated by these studies.

Blind Mole Rats. The mole rat is a rodent that spends its entire life in totally dark, underground tunnels. Such an animal has no use for a light detection system, and its eyes are covered with furry skin. In spite of its covered eyes, it does possess a dorsal division of the lateral geniculate nucleus and striate cortex. At birth, the retina projects to the lateral geniculate nucleus, but this pathway soon degenerates and stimulation of the eyes with light does not result in the generation of electrical activity in its striate cortex. Blind mole rats, however, depend heavily on the auditory system for information about the external environment. The remarkable characteristic of blind mole rats is that neurons from the auditory system invade the idle visual system and convert its functions to auditory processing. Thus, the pars dorsalis of the lateral geniculate nucleus

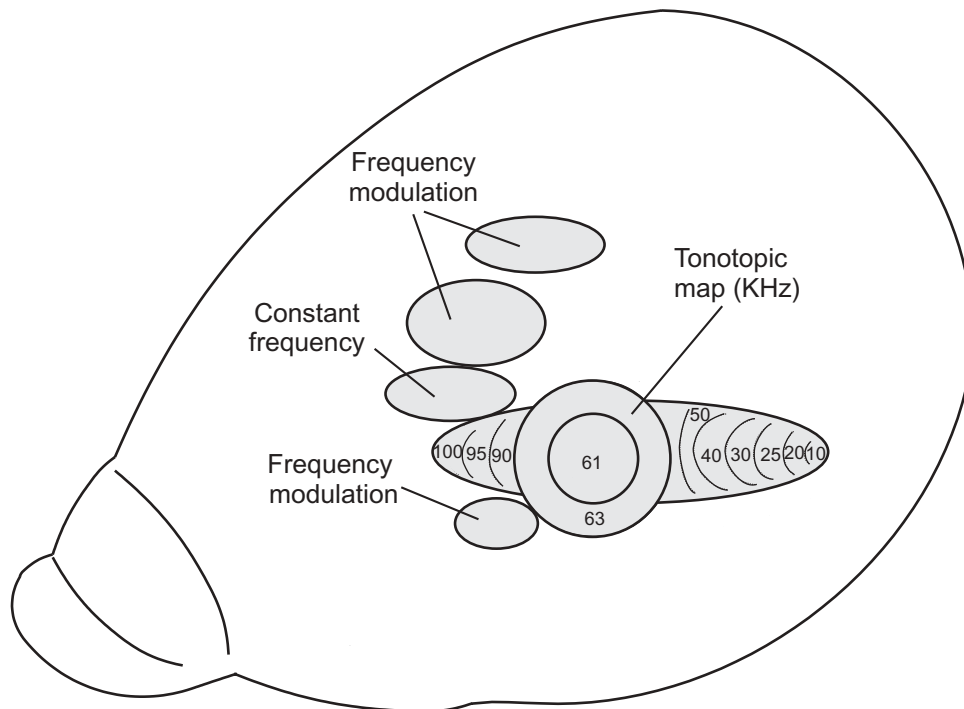


FIGURE 28-9. Some of the major areas of the auditory cortex of the mustache bat, including a large tonotopic map and specialized areas for the detection of constant-frequency and frequency-modulated tones. Based on data from Suga (1984).

as well as the striate cortex of mole rats are responsive to auditory stimulation. This “invasion” of a neighboring sensory system may offer an important clue to one of the mechanisms of sensory system evolution.

Connections of the Auditory Cortex. The connections between the auditory cortex and the auditory dorsal thalamus of a cat are shown schematically in Figure 28-10. The figure shows three regions of auditory cortex: A1, A2, and a region described as the auditory belt, which varies considerably between species and contains a number of subdivisions that are not always contiguous. In general, however, the principal source of afferents to A1 is the ventral division of the medial geniculate nucleus. The magnocellular division has a very widespread projection and sends its efferents to virtually all auditory cortical areas. Axons originating in the dorsal division of the medial geniculate nucleus mainly terminate in the auditory belt region that surrounds A1 and A2. The auditory cortical areas, like those of the somatosensory and visual cortices, are interconnected with each as shown in the figure. In addition, A1 sends efferent axons to the ventral division of the medial geniculate nucleus as well as to the inferior colliculus, which constitutes the auditory midbrain of mammals.

Reptiles and Birds

As with somatosensory and visual collothamic pathways from the dorsal thalamus to the telencephalon in reptiles and birds, the target of the auditory collothamic pathway is the

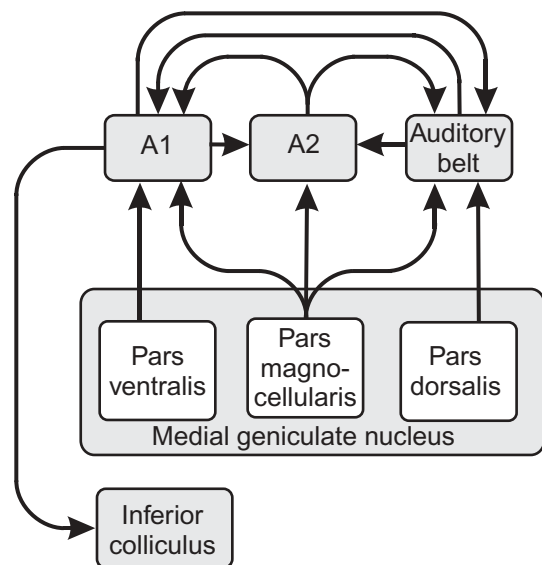


FIGURE 28-10. Major connections of the auditory cortex of a cat.

dorsal ventricular ridge. In the case of the auditory pathway, the termination field is in (or very near to) the medial wall of the dorsal ventricular ridge, as illustrated in an iguana (Fig. 28-11), a turtle (Fig. 28-12), and a pigeon (Fig. 28-13).

The telencephalic auditory area in the dorsal ventricular ridge in birds is more complex than in reptiles. This area is

known as Area L pallii, formerly known as Field L, based on the telencephalic nomenclature of the avian telencephalon proposed by Maximilian Rose, in which he designated the various regions of the telencephalon with letters of the alphabet rather than names such as entopallium or nidopallium. The merit of Rose's system is that it is completely neutral and implies nothing about homologies with structures in the brains of mammals or other vertebrates. Its disadvantage is that names (even if they later may turn out to be inappropriate or misleading) are easier to associate with a region of the brain than are letters of the alphabet. This is particularly true when some notion of homology or equivalence is inherent in the name. Rose's nomenclature never achieved popularity among researchers except for Field L (now area L pallii), for which there was no specific preexisting name.

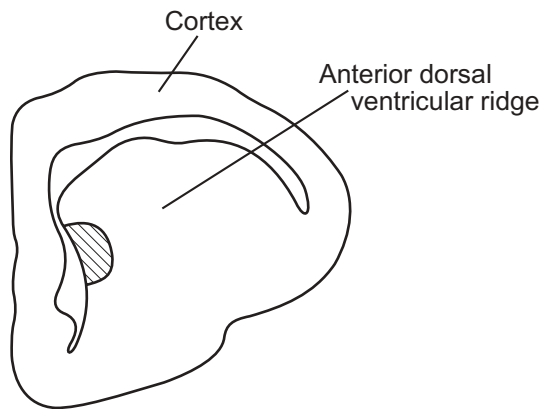


FIGURE 28-11. Drawing of a transverse hemisection through the telencephalon of a lizard. The auditory projection area within the dorsal ventricular ridge is indicated by diagonal lines. Adapted from Bruce and Butler (1984).

Figure 28-13 also shows that area L pallii consists of three laminae: **L1**, **L2**, and **L3**. The thalamorecipient layer of area L pallii is L2; different regions within lamina L2 receive the ascending axons from nucleus ovoidalis. Laminae L1 and L3 are interconnected with L2. Figure 28-14 shows a schematic representation of the columnar and tonotopic organization in area L pallii. The figure indicates that each lamina of area L pallii contains its own tonotopic organization.

Figure 28-15 summarizes the pathways of the auditory forebrain in amniotes. The figure shows the pathways in mammals, reptiles, and birds. In each, the axonal pathway from the thalamic auditory nucleus (the medial geniculate nucleus, the reuniens-medialis complex, or the nucleus ovoidalis) is shown to its respective telencephalic target (auditory cortex, the auditory area of the dorsal ventricular ridge, or area L pallii). In each class, only a collothamic pathway has been reported.

VOCAL TELECEPHALON

The emission of sounds from the oral cavity is a characteristic of many vertebrate species, especially those animals that live in air. Air-breathing animals are well adapted for this behavior because of the relative ease of manipulation of the air column that is moving in and out of the body for respiration. This is much the way the performer on a musical wind instrument manipulates the air column within the instrument by blowing and operating various valves or tube lengths to produce different musical notes. The sounds made by air-breathing animals, known as **vocalizations**, serve a variety of purposes such as establishment and defense of territories, attraction of mates, intimidation of rivals, contact with mates or young when not in view, and warning others of the presence of predators and other dangers. Although these forms of communication carry considerable information for the

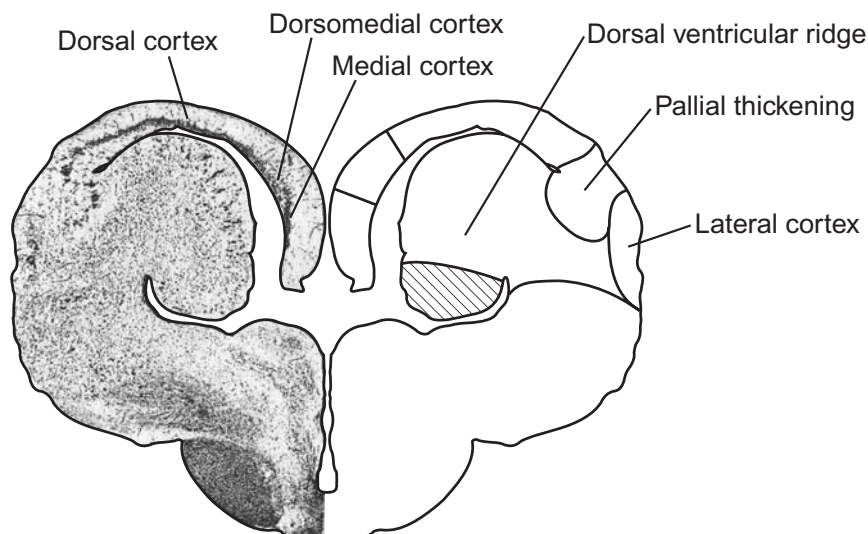


FIGURE 28-12. Transverse hemisection with mirror-image drawing through the telencephalon of a turtle. The auditory projection area within the dorsal ventricular ridge is indicated by diagonal lines. Adapted from Balaban and Ulinski (1981) and used with permission of John Wiley & Sons.

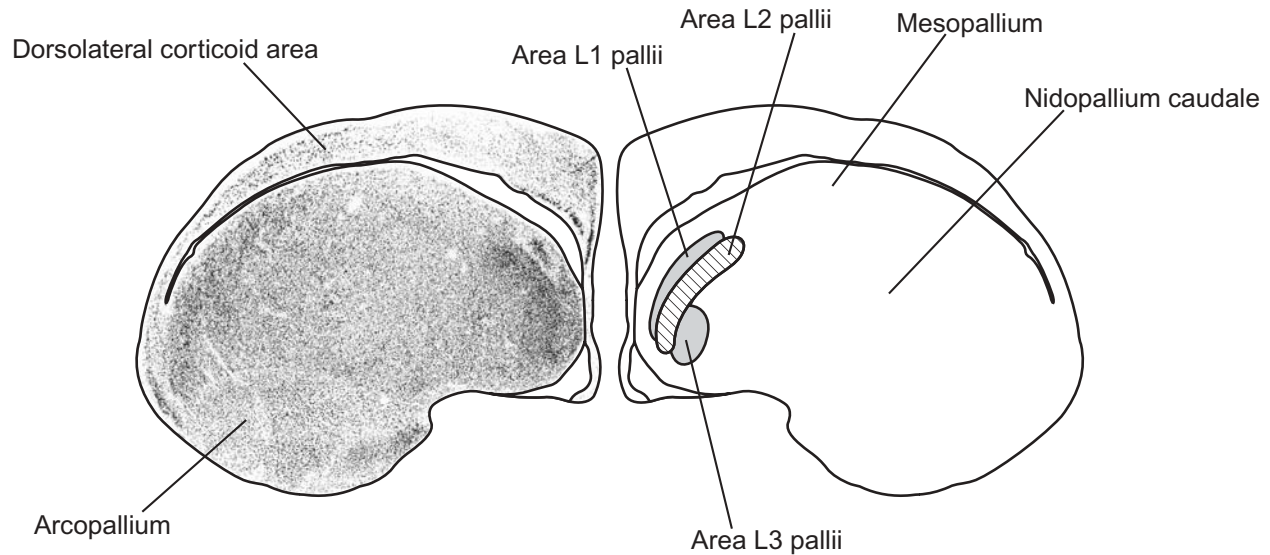


FIGURE 28-13. Transverse hemisection with mirror-image drawing through the diencephalon of a pigeon. The auditory area (L2) and its related regions (L1 and L3) within the nidopallium of the dorsal ventricular ridge are indicated by diagonal lines and shading, respectively. Adapted from Karten and Hodos (1967) with additional data from Wild et al. (1993). Used with permission of The Johns Hopkins University Press.

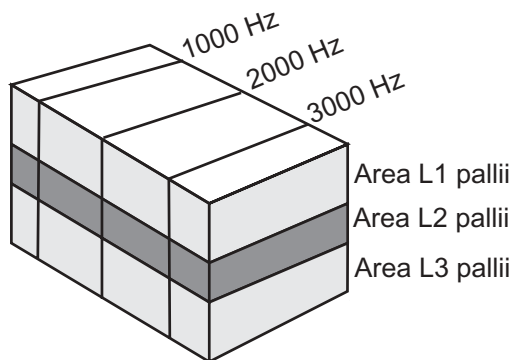


FIGURE 28-14. Tonotopic and columnar organization in area L pallii of a bird.

listener, they do not constitute language because they lack grammatical rules of sentence structure such as subject and object. Only humans are capable of vocal language. Until recently, humans were thought to be the only animals that are capable of language of any sort, vocal or otherwise. Recent studies of chimpanzees have shown that these animals, which are generally believed to be the closest primate relatives to humans, have the capacity to learn and use nonvocal language in the form of manipulation of symbols or through the use of American sign language, such as is used by hearing- or speech-impaired humans. These animals also demonstrate an ability to understand the grammatical content of human speech, rather than merely responding to spoken commands such as we might use with a pet dog or some other domestic animal. Although these observations are impressive, some controversy surrounds

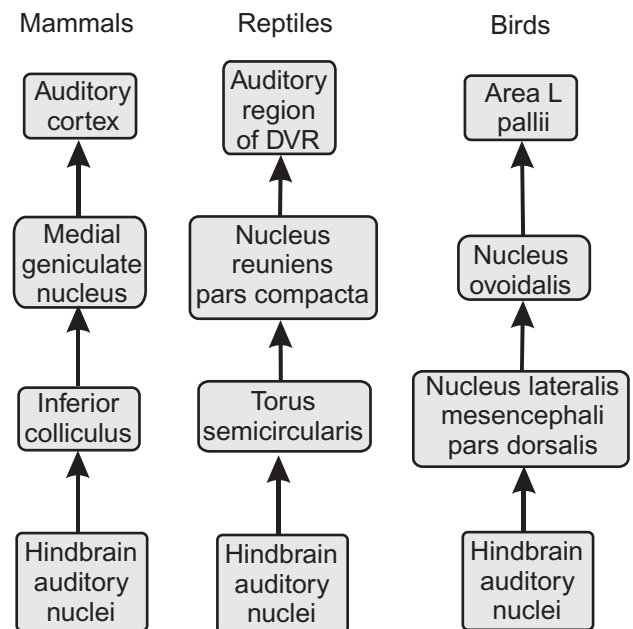


FIGURE 28-15. Summary of the auditory forebrain in mammals, reptiles, and birds.

the interpretation of this research, and some experts in human language remain unconvinced.

Vocalization and Hearing

Hearing is closely related to vocalization for several reasons. First, affecting the behavior of another animal is almost

invariably the purpose of vocalization; if the vocalization is not heard, it cannot have an effect. Second, hearing is important for the development and maintenance of vocalization in many animals. The vocalizer hears its own vocal productions and therefore can modulate or modify them in accordance with the situation.

For most animals, the pattern of their vocalizations is innate and species typical. However, many species of birds learn their calls during early posthatch development by listening to their parents vocalize as well as listening to their own sound. Likewise, humans learn articulate speech not only by listening to other humans speaking but also by listening to their own vocal productions.

Figure 28-16 presents an overview of amniote vocal-respiratory pathways. The pathway consists of a telencephalic region that initiates the sequence. This is followed by a cascade of command generators located in the midbrain and hindbrain. The hindbrain command generators direct the activity of three groups of premotor and motor neurons: (1) a respiratory pathway that controls the muscles of respiration; (2) a tongue, larynx, and syrinx (in birds only) pathway; and (3) a mouth and jaw pathway.

Anurans

As noted above, although this chapter addresses the auditory and vocal forebrain in amniotes, a brief digression on anurans is included here since the system has been well studied in these animals by Catherine Brahic and Darcy Kelley and has a number of similarities to those of birds and mammals. Frogs produce their vocalizations in a manner somewhat different from that of other tetrapods. Air is drawn into the pharynx by negative pressure caused by the animal lowering its pharyngeal floor. Air flowing through the pharynx inflates an elastic sac, known as the **vocal sac**. This sac is formed in the floor or lateral wall of the pharynx. The sac resonates as the air passes over the animal's vocal cords producing the animal's vocalization.

Figure 28-17 illustrates the vocal-respiratory pathway in frogs. Figure 28-17(A) shows the pathways in a frog of the genus *Rana*, and Figure 28-17(B) shows the pathways in *Xenopus laevis*. The telencephalic area is the ventral striatum, which sends a descending pathway to a hindbrain command generator known as the **pretrigeminal nucleus** in *Rana* and the **pretrigeminal nucleus of the dorsal tegmental area of the medulla** in *Xenopus*, which projects, via the reticular

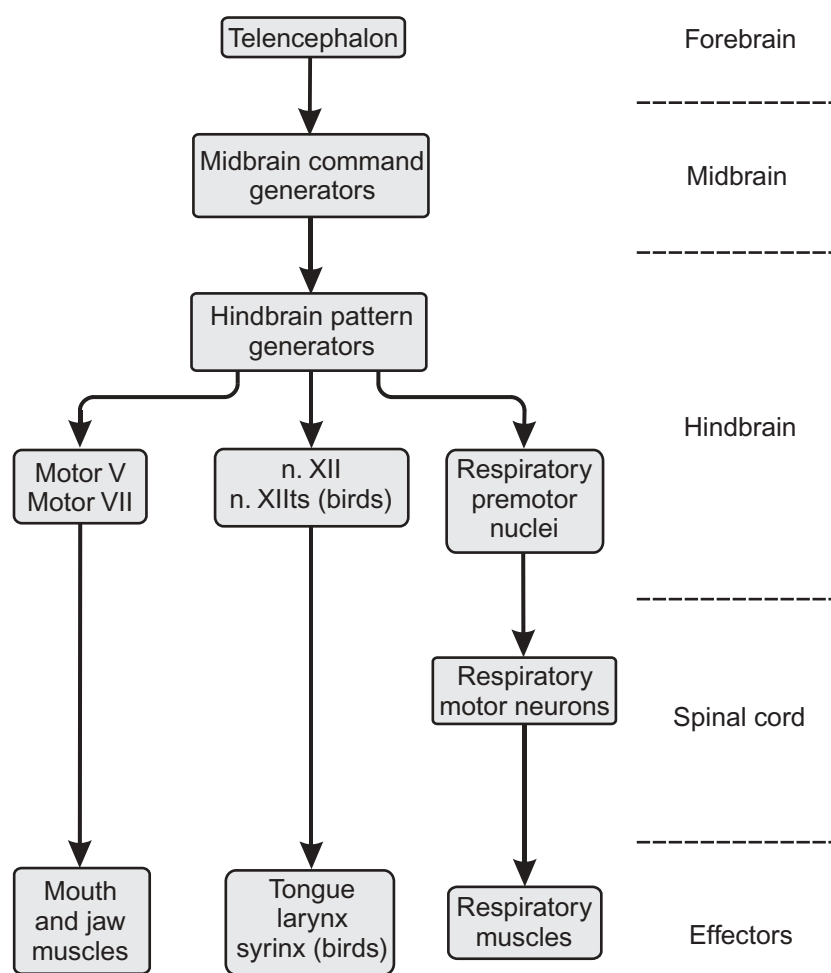


FIGURE 28-16. Amniote vocal-respiratory pathways.

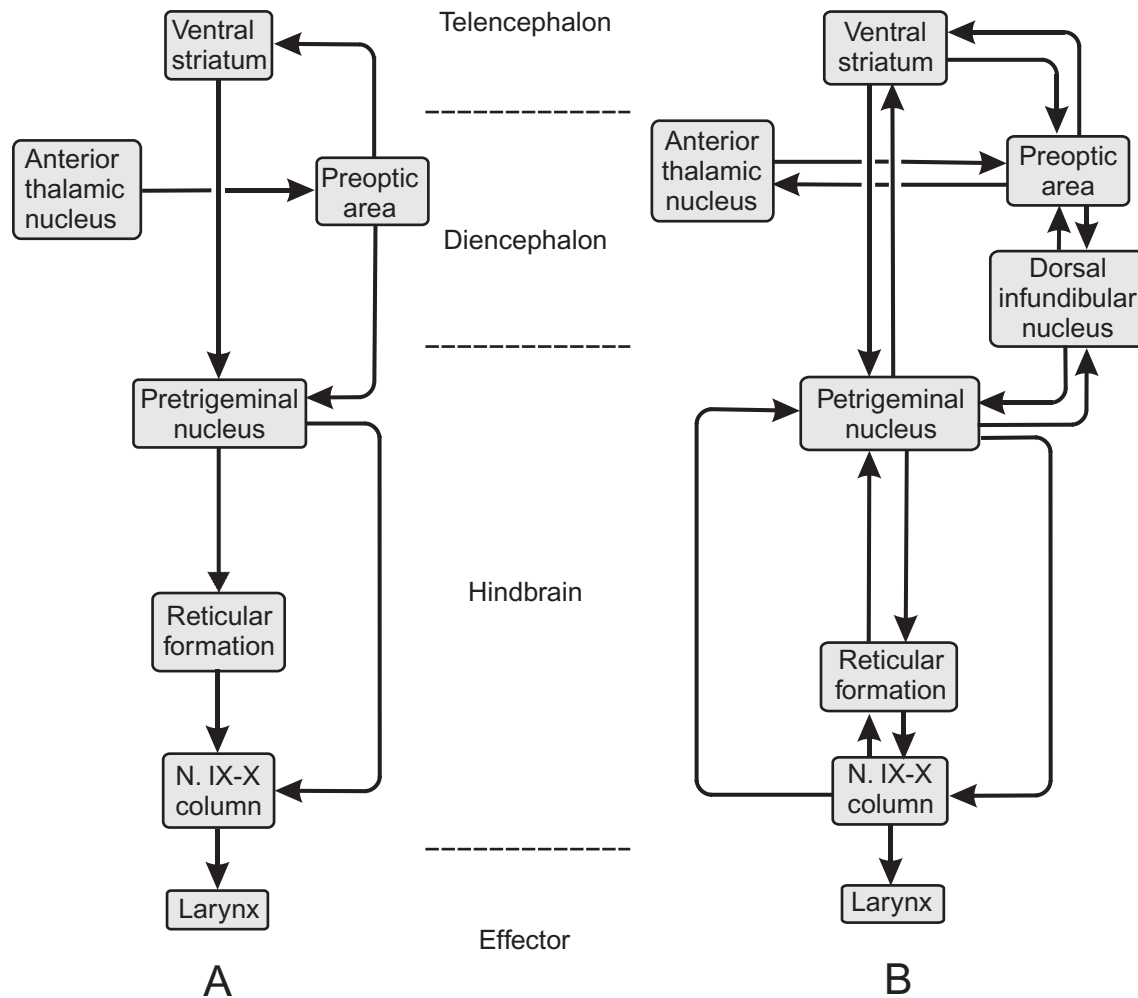


FIGURE 28-17. Vocal control pathways in frogs. A: *Rana*. B: *Xenopus*, based on Brahic and Kelley (2003).

formation, to motor neurons in the glossopharyngeal-vagal column in the hindbrain and then to the larynx. Other parts of the system are the **preoptic area** in both *Rana* and *Xenopus* and the **dorsal infundibular nucleus** in *Xenopus*. Note the many reciprocal connections among the components of this system in *Xenopus*. Physiological studies have shown that the vocal pathway has short latency responses to stimulation of auditory nuclei, such as the anterior thalamic nucleus shown in *Xenopus*.

Reptiles and Birds

Relatively little research has been done on the vocal control mechanisms of reptiles. This is perhaps due to reptilian dependence on visual and olfactory signals for communication. Some reptiles do emit vocalizations, such as hisses, chirps, and/or other distinctive communication sounds. However, their repertoire is rather limited in contrast to the rich variety of vocal signals produced by mammals and the extraordinary complexity of vocalizations of which humans and birds are capable.

The vocal-control system of birds, especially in songbirds, such as canaries and finches, has been the subject of considerable attention by neuroscientists during the past three decades. Substantial progress has been made in mapping the axonal pathways from the telencephalon to the nucleus of the hypoglossal nerve (cranial nerve XII) in the caudal hindbrain, a portion of which controls the organs of vocalization. The organ of vocalization in birds is called the **syrinx**, the Greek word for "whistle," and it is located at the bifurcation of the trachea. The nucleus in the hindbrain that controls the syrinx is the **tracheosyringeal division of the hypoglossal nucleus** of cranial nerve XII, otherwise known as **nucleus XII_{ts}**. This division of nucleus XII contains the motor neurons that control the muscles of the trachea and syrinx. Figure 28-18 shows the forebrain pathways that link the auditory system with the vocal-respiratory control pathways in two highly vocal birds. Figure 28-18(A) shows the two main forebrain pathways that have been described in a song bird, and Figure 28-18(B) shows the pathways in a parrot. The reader should note that the nomenclature of the avian vocal control nuclei of the telencephalon has undergone a complete transformation as

cephalic **nucleus interfascialis nidopallii**. The importance of HVC for vocal behavior may be seen in the strong relationship between the volume of HVC and the number of song types that a songbird species typically has in its repertoire: the more song types, the greater the volume of HVC. Axons from HVC pass to the **nucleus robustus arcopallii (RA)**, formerly known as the robust nucleus of the archistriatum, which is located in the region of the telencephalon that gives rise to other descending pathways that are presumed to be motor. This pathway appears to control the initiation and production of vocalization. A second output pathway from HVC is to the telencephalic **area X**, which then projects to RA by a circuitous route. Area X projects to the mesencephalic nucleus, **nucleus dorsomedialis**, which then projects to the telencephalic **nucleus lateralis magnocellularis nidopallii anterioris (LMAN)**, formerly called the lateral part of the anterior magnocellular nucleus. LMAN in turn projects to RA. RA gives rise to descending projections to the nucleus Xlts and to the respiratory pathway in the hindbrain.

Area X demonstrates a **sexual dimorphism** such that it is well developed in male songbirds but does not appear as a distinct morphological entity in females (see Box 28-1). In males, the projection from HVC to area X is substantial; in females a modest projection from HVC terminates on neurons in the region in which area X is found in males, even though area X does not stand out from the surrounding neurons in females as it does in males. This sexual dimorphism is consistent with the observation that male songbirds have a greater number and a richer variety of songs in their repertoires than do female songbirds. This second pathway, from HVC to RA via the area X-nucleus dorsomedialis-LMAN route, appears to be related to the learning and memory of song.

Figure 28-18(B) shows the vocal-respiratory control pathways in a budgerigar, which is a small parrot. These pathways have an organization that bears an overall similarity to those of the songbird but with a number of significant differences in structures and in nomenclature. An interesting feature of the

parrot pathway is that the auditory input to the parrot's presumed equivalent structure to HVC, the **nucleus centralis nidopallii lateralis**, previously called the central nucleus of the lateral neostriatum, does not come directly from area L pallii but rather by way of the **nidopallium frontale pars lateralis**, formerly called the neostriatum frontale pars lateralis. An additional auditory input comes by way of the **nucleus basorostralis pallii**, the former nucleus basalis, of the telencephalon, which we encountered in our discussion of the trigeminal somatosensory system in birds in Chapter 27.

Two routes to the **nucleus centralis arcopallii anterioris**, previously called the central nucleus of the anterior archistriatum, and which seems comparable to the RA of songbirds are present. The first is from the **nucleus centralis nidopallii lateralis**, the former central nucleus of the lateral neostriatum, and thence to the vocal and respiratory nuclei of the midbrain, hindbrain and spinal cord. The second route is from the **magnocellular nucleus of the dorsomedial thalamus**, which receives its input from a complex set of pathways comprising the **nucleus ovalis mesopallii**, formerly the oval nucleus of the ventral hyperstriatum, the **nucleus ovalis nidopallii anterioris pars medialis**, the former medial part of the oval nucleus of the anterior neostriatum, and the **striatum mediale pars magnocellularis**, which was the former magnocellular nucleus of the lateral paleostriatum.

Figure 28-19 illustrates the vocal-control pathway in a non-songbird. Note the relative lack of complexity in this pathway compared with songbirds or birds that learn a variety of vocalizations throughout their lives, such as parrots.

Figure 28-20 shows a further set of descending auditory pathways in songbirds and pigeons that illustrate the intimate relationship between the vocal system and the auditory system. These pathways include a region known as the **shelf**, which is located immediately ventral to the HVC. The efferents of the shelf are to a group of neurons known as the **cup** of the arcopallium, situated rostral and dorsal to the nucleus robustus of the arcopallium (RA).

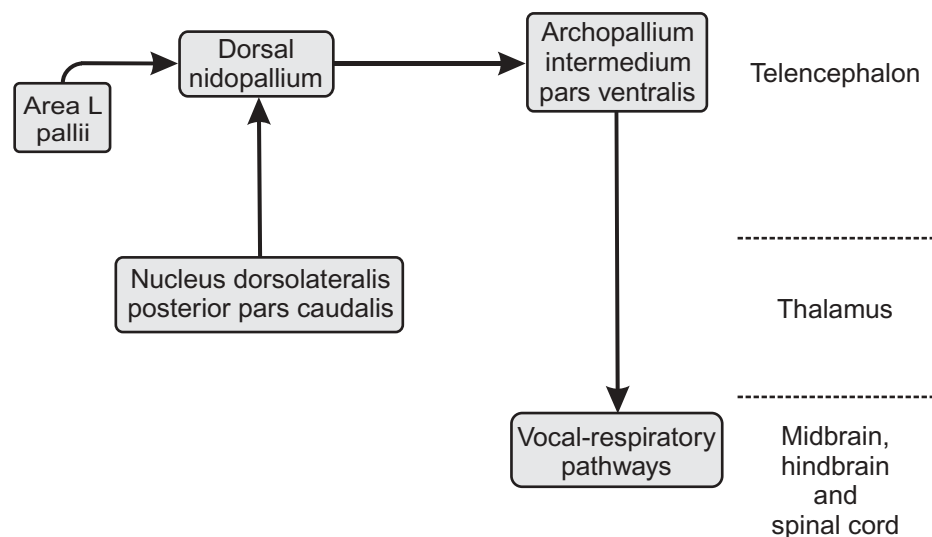


FIGURE 28-19. The vocal control pathway in a non-songbird.

BOX 28-I. Sexual Dimorphism in the Auditory and Vocal Control Systems

Of the many functions of vocal communication, its role in courtship is paramount among the oscine birds, which are those species generally characterized as songbirds. Male song serves to attract mates and to maintain the male-female pair bond. In some species, such as zebra finches (*Taeniopygia guttata*), in which the males sing whereas the females do not, this behavioral difference correlates with a dramatic sexual dimorphism in the telencephalic vocal control nuclei and in brain stem vocal and auditory nuclei as well.

In general, the degree to which sexual dimorphism of the auditory and vocal control systems occurs in various oscine species depends on the extent to which there is a behavioral difference in vocal capability between males and females. This in turn is determined by male-female differences in estradiol early in ontogenetic development, which affects differential cell death and other differences as well. Testosterone may contribute to later differentiation of the system in males and females. In contrast, in species in which both males and females sing in more or less equal amounts, sexual dimorphism is minimal. Finally, in birds such as the European starling (*Sturnus vulgaris*), in which females sing, but to a lesser extent than the males, an intermediate sexual dimorphism has been observed.

Included among the telencephalic areas that show sexual dimorphism in songbirds are HVC, the robust nucleus of the arcopallium (RA), and area X. In addition, the motor neurons of the tracheo-syringeal division of the hypoglossal nerve (nucleus XII_{ts}), which controls the muscles of the larynx and syrinx, also shows a difference between males and females in response to auditory stimulation and electrical stimulation of HVC.

Among the differences reported between the sexes in telencephalic song nuclei are differences in cell number, the volume of the nuclear groups, and the number of cells that are targets of steroid hormones, as well as histochemical differences in such neuroactive substances as norepinephrine, dopamine, nitric oxide, substance P, somatostatin, calcitonin gene-related peptide (CGRP), melatonin, and others. Although nucleus lateralis magnocellularis nidopallii anterioris (LMAN) appears grossly similar in both males and females, in zebra finches at least, males exhibit characteristic changes in synapse number and synaptic contact length that the females do not.

Some amphibians also show sex differences in vocal behavior during courtship. The neuronal populations of the vocal control pathway in *Xenopus* shows a sexual dimorphism as does the peripheral sound-producing apparatus. In this instance, the sexual dimorphism and behavioral differences are under the control of androgenic rather estrogenic hormones as in birds. In tree frogs of the genus *Hyla*, the sexual dimorphism extends to the auditory system as well.

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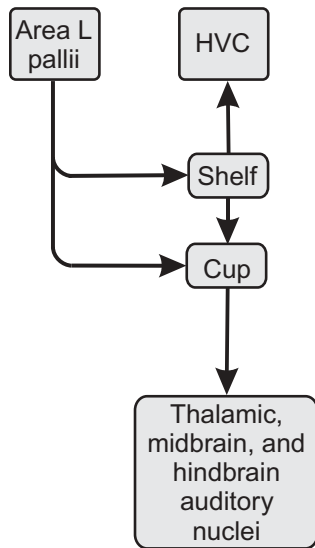


FIGURE 28-20. Descending auditory pathways from area L pallii in birds and their relationship to telencephalic vocal control nuclei.

Both the shelf and the cup receive projections from area L pallii. The efferents of the cup are to auditory nuclei of the thalamus (nucleus ovoidalis), the midbrain (MLd), and the hindbrain auditory nuclei.

Mammals

Although the great majority of mammals vocalize to a greater or lesser extent, the mammals most studied in this regard are humans because of the importance of speech and language disturbances after various types of head injuries, strokes, and other types of neurological disorders. An area at the caudal end of the left inferior frontal gyrus was identified by the nineteenth century French surgeon Pierre Paul Broca as an area of cortex, now known as **Broca's area**, which is responsible for motor control of speech. This area corresponds to Brodmann's area 44 and the adjacent part of area 45. Broca's area is adjacent to the part of motor area M1 that controls movements of the mouth, face, lips, and tongue.

Patients with damage to this region exhibit a disorder known as **aphasia**, which is the inability to express themselves by speech. Broca's aphasia, which is a motor aphasia, should be distinguished from Wernicke's aphasia (named for Karl Wernicke, a nineteenth century German psychiatrist), which is a sensory aphasia that is manifested by an inability to understand speech. The cortical area in which damage results in Wernicke's aphasia, known as **Wernicke's area**, is located in the left temporal lobe, immediately caudal to the A1 auditory cortex. This area is equivalent to the posterior third of Brodmann's area 22. Damage to these areas also can affect both the comprehension and production of written language. Wernicke's area and Broca's area are interconnected by a major intratelencephalic axon bundle known as the **arcuate fasciculus**, which is so named because of the arc that it forms as it first runs caudally to leave the temporal lobe and then swings rostrally to enter the ventral frontal lobe. Other areas that have

been reported to be involved in the production of vocalization are the supplementary motor area, the anterior cingulate cortex, and the periaqueductal gray. That language functions and certain other psychological functions are located predominantly in the right or left hemisphere rather than being distributed with bilateral symmetry, as are the majority of neural functions, which has led to the concept of **hemispheric dominance (specialization)** or **cerebral dominance**. A discussion of this interesting concept would take us too far afield from the purposes of this book. Thus we can do no more here than to call it to your attention and refer you to the list of further readings at the end of this chapter.

In mammals, the production of vocal sounds is carried out by the **larynx**, which is a chamber composed of cartilage and several sets of muscles. The movement of the respiratory air column is modulated by various muscles and also resonates in the mouth cavity to produce vocal sounds. Vocalizations can also be varied by changing the size and shape of the mouth cavity by adjustment of the jaws, lips, and tongue. The muscles of the larynx are innervated by motor neurons of the **nucleus ambiguus**, which is located in the caudal hindbrain. These neurons project to the larynx via the vagus nerve. The jaw, lip, and tongue muscles receive their innervation from the motor nuclei of the trigeminal, facial, and hypoglossal nerves. The actions of these four sets of hindbrain motor nuclei are coordinated by the reticular formation of the pons and medulla.

The vocal control pathway of humans originates in Broca's area and other areas of motor cortex, which include the supplementary motor area (M2) and the medial premotor area in the cingulate cortex (Brodmann's area 24). Neurons in these areas send their axons via the corticobulbar tract to motor V, motor VII, nucleus XII, and the nucleus ambiguus. A second pathway, which appears to be involved in the emotional aspects of speech, originates in the anterior cingulate cortex and involves a variety of limbic system structures; this pathway passes to the midbrain command generator, which is in the periaqueductal gray, and then to the hindbrain and spinal cord pathways for respiration and vocal control. The sensory and motor pathways for speech, respiration and vocalization in humans are shown in Figure 28-21.

Figure 28-22 shows the details of the vocal-respiratory pathways in a songbird and in a human. Despite differences in nomenclature, an impressive similarity may be seen in the two pathways.

An important distinction must be made between speech and vocalization. Virtually all mammals are capable of vocalization, and some, such as humans, bats, and aquatic mammals, are capable of vocal learning. Only humans, however, possess that special type of vocalization that we refer to as speech. Only humans use Broca's area and Wernicke's area for producing and understanding speech. In nonhuman mammals, telencephalic control of vocalization is carried out by the supplementary motor area (M2) and the anterior cingulate cortex (Brodmann's area 24). Electrical stimulation of the region in nonhuman primates, the ventral premotor area, that corresponds to Broca's area in humans results in movements of the oral region of the face but not actual vocalization. In contrast, in many mammals and other tetrapods as well, vocalization results from stimulation of regions in the **periaqueductal gray** area of the dorsal midbrain tegmentum. In humans, the periaque-

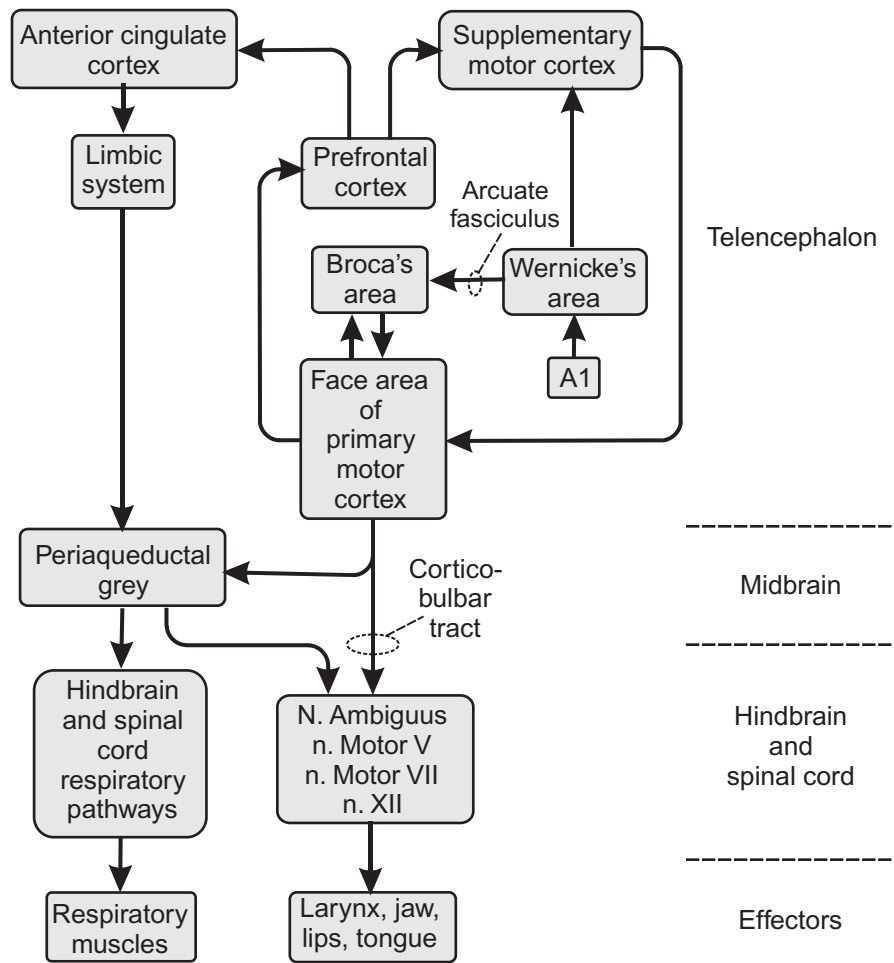


FIGURE 28-21. Vocal control pathways in humans.

ductal gray vocalization pathway is associated with involuntary vocalizations such as those produced during emotional states of pain or pleasure.

EVOLUTIONARY PERSPECTIVE

Auditory pathways in reptiles and birds follow a consistent pattern of a collothamic pathway from the auditory midbrain to a dorsal thalamic auditory nucleus to the medial dorsal ventricular ridge. The mammalian pattern is consistent with this overall plan; the thalamic auditory nucleus has several divisions that have different terminal fields in auditory neocortex. A lemnothalamic auditory pathway that passes from the auditory receptive nuclei of the hindbrain directly to the thalamus, thus bypassing the auditory midbrain, has not been described in any vertebrate. The absence of such a pathway may be related to a major difference between the topographic organization of the auditory pathway and that of the somatosensory and visual pathways, namely, that the auditory topography is tonotopic; that is, each region of the topographic map represents a certain number of cycles of the acoustic wave per second. In contrast, the visual and somatosensory topographies are spatial topogra-

phies based on visual space and space on the body surface. A speculative possibility is that spatial topographies require a lemnothalamic organization plus a collothamic organization, whereas a tonal topography can make do with only a collothamic organization. Perhaps future research will shed light on this possibility. A second possible explanation may lie in the fact that vestibular projections to the dorsal thalamus are direct, and this system may represent the lemnothalamic component of the octaval system.

A consistent pattern also can be seen in the evolution of the vocal-control pathways. The portion of the pathway that seems common to mammals, reptiles, and birds is control of vocalization by the periaqueductal gray region of the dorsal tegmentum in the region of the junction between the midbrain and pons, although there is some disagreement as to whether the nucleus dorsomedialis is the homologue of the periaqueductal gray. This area probably acts to influence the motor nuclei of the hindbrain that control vocalization. Two groups of amniotes have evolved additional neuronal networks that control the vocalization-control system. In mammals, because the size and shape of the oral cavity affects vocalization, those motor nuclei that affect oral-cavity size and shape (trigeminal, facial, and hypoglossal) are participants in this system.

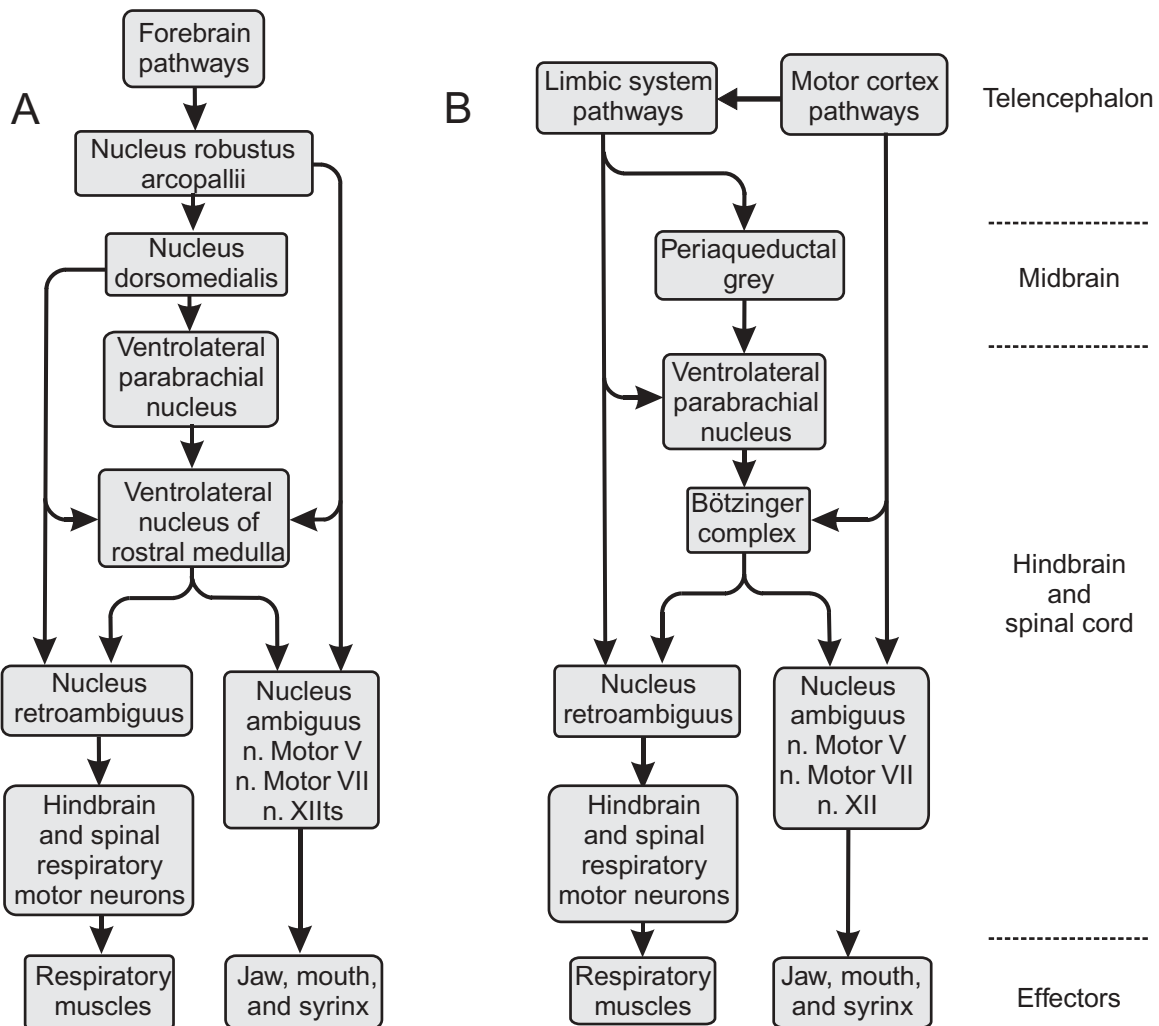


FIGURE 28-22. Comparison of vocal and respiratory control pathways in songbirds (A) and humans (B).

Mammals have evolved specialized regions of neocortex that each have a detailed topography of the body including the face and oral region. These motor areas exert control over the motor nuclei of the brainstem. Humans, which are the only animals that are capable of molding their vocalizations into speech, have an additional specialized motor-speech area near the face region of M1 that is important for the production of speech sounds.

Birds differ somewhat from mammals in that they lack lips and are relatively incapable of affecting oral cavity size and shape, except by opening and closing the beak. Birds have a specialized vocal organ, the syrinx (in addition to a larynx), but only the hypoglossal nucleus, a portion of which controls the muscles of the syrinx, is involved. Although avian vocalizations do not have the cognitive and linguistic content of human speech, they nevertheless have an extremely rich complexity and variability, especially among songbirds. The avian vocal-control pathways have evolved independently of those in mammals, with many similarities and some differences. Parrots and songbirds, both capable of complex vocalizations and rich

vocal repertoires, have each independently developed complex forebrain circuitry that differs in a number of ways from one another. Hummingbirds also produce complex vocalizations and likewise have complex forebrain circuitry that supports this behavior.

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Terminal Nerve and Olfactory Forebrain

INTRODUCTION

Most vertebrates have two rostral nerves: the **olfactory nerve** and the **terminal nerve**. Some tetrapods have a third rostral nerve, the **vomerolnasal nerve**, in addition to the olfactory and terminal nerves. The olfactory and vomeronasal nerves, along with the sense of taste, constitute the chemosensory system. The modality of the terminal nerve has not yet been established.

The rostral chemosensory nerves are composed of the axons of **bipolar receptor cells** that, along with secretory supporting cells, form the olfactory epithelium of the nasal cavities. Their axons terminate within the most rostral parts of the brain. The olfactory nerve terminates within the **olfactory bulb** in fishes. In some tetrapod taxa, the site of termination of the olfactory nerve is called the **main olfactory bulb** to distinguish it from the site of termination of the vomeronasal nerve, the **accessory olfactory bulb**. The collections of axons that originate in the olfactory bulb(s) and project to areas within the rest of the brain are referred to as tracts. Thus, in mammals, for example, the olfactory nerve terminates in the main olfactory bulb, and the main olfactory bulb gives rise to the **olfactory tract**, which terminates in the **olfactory cortex** in the telencephalon. The parts of the pallial amygdala that receive main olfactory bulb projections often are considered to be part of the olfactory cortex. Where present, the accessory olfactory bulb projects to other parts of the pallial amygdala and to the medial amygdala as well, which is a subpallial nucleus.

In this chapter, we will first discuss the organization of the olfactory nerve system in Group I and Group II vertebrates.

Then we will discuss the vomeronasal nerve system in tetrapods. The system that involves the terminal nerve differs somewhat in its organization and functional role from the other two rostral nerve systems and will be discussed last. The terminal nerve system will first be discussed in general terms for vertebrates, and then its special features in teleosts will be considered.

OLFACTORY SYSTEM

The olfactory nerve arises from neurons in the olfactory epithelium that have dendritic endings specialized for the detection of chemical stimuli and that project into the olfactory bulb. The paired olfactory bulbs are formed by evagination during development, whether the telencephalic hemispheres are formed by evagination, as in most vertebrate groups, or by eversion, as in ray-finned fishes.

The olfactory input through the olfactory bulbs is a two-neuron relay system in which the receptor cells project to cells called **mitral cells** (for their resemblance to a bishop's mitre) within the olfactory bulb (Fig. 29-1). The multiple ramifications of both the axon of the receptor cell (R) and the dendrite of the mitral cell (M) form a complex sphere, called a **glomerulus** (G), where they meet, like the joining of two hands with the fingers partially flexed and intermingled. **Granule cells** (Gr) are also present in the olfactory bulb, and along with centrifugal inputs from the forebrain, influence the processing of olfactory information in the bulb.

The olfactory bulbs relay olfactory information to the olfactory pallium via the olfactory tracts. The relative lengths of both the olfactory nerves and the olfactory tracts are

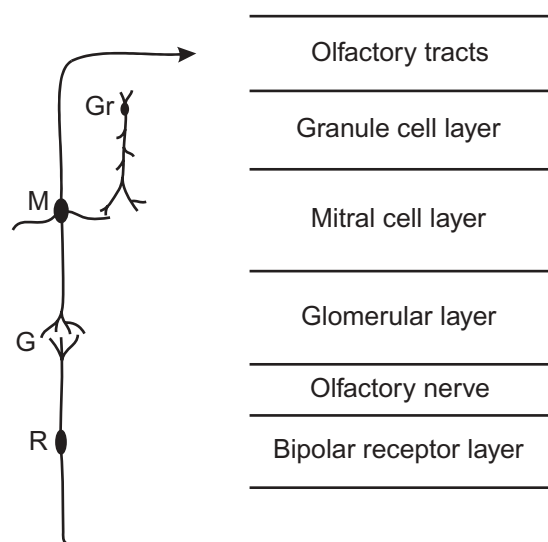


FIGURE 29-1. Olfactory bulb organization in vertebrates: schematic drawing of an olfactory bipolar receptor cell (R) with its axon terminating in a glomerulus (G) formed by the receptor axon terminals and the distal branches of the dendrite of a mitral cell (M), which in turn projects to the olfactory cortex (arrow). A granule cell (Gr) is also shown terminating on a dendrite of the mitral cell.

variable. In many vertebrates, including some cartilaginous and bony fishes, the olfactory bulbs are sessile in position, that is, they are juxtaposed to the telencephalon. In these cases, the olfactory nerves may be of shorter or longer length, depending on the distance of the olfactory epithelium from the olfactory bulbs. In other cartilaginous and bony fishes, the olfactory bulb lies close to the olfactory epithelium, and the olfactory tract is an elongated structure running between the olfactory bulb and the telencephalon.

The olfactory pallium is usually thought of as a distinct cytoarchitectonic area in the telencephalon that has afferent olfactory innervation, but such a working definition is acceptable only as a first approximation. Other criteria, such as topology, cytoarchitecture, efferent projections, and histochemical characteristics, also are important in defining and distinguishing pallial areas, but data on these aspects of the olfactory system in anamniotes are limited. Olfactory fibers terminate in more than one distinct pallial area in a number of anamniotes, and some of these areas appear to be part or all of the dorsal pallium on topological, cytoarchitectonic, and/or histochemical grounds. However, due to the relative dearth of information on the latter features and on efferent connections of these pallial areas, identifying them as homologues of specific pallial areas in amniote vertebrates is somewhat hazardous.

Among the telencephalic regions in amniotes that receive olfactory inputs relayed from the olfactory bulb(s) is a subset of a group of nuclei, collectively called the amygdala. Parts of the pallial amygdala receive input from the main olfactory bulb. In most tetrapods, another part of the amygdala receives direct vomeronasal input from the accessory olfactory bulb. The main olfactory-recipient and vomeronasal-recipient parts of the amygdala are considered in this chapter. The subpallial com-

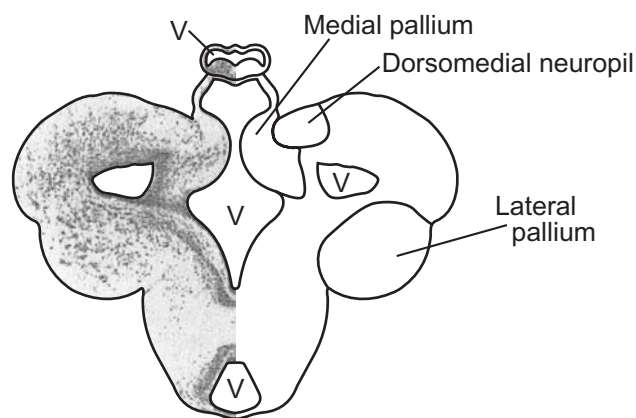


FIGURE 29-2. Transverse hemisection with mirror-image drawing through the telencephalon of a lamprey (*Ichthyomyzon unicuspis*). Adapted from Northcutt and Wicht (1997) and used with permission of S Karger AG, Basel.

ponents of the amygdala were discussed in Chapter 24, and its nonolfactory, frontotemporal division was discussed in Chapter 25.

Group I

In lampreys, the olfactory bulbs contain a **glomerular layer** that lies deep to the olfactory nerve fibers, a **layer of mitral cells**, and a **granular cell layer** that contains cells of varying morphology. Axons from cells in the granular cell layer contribute to the olfactory tracts along with the mitral cell axons. Olfactory bulb projections are dense within a large area in the telencephalon, which has been identified as the **lateral pallium** (Fig. 29-2) partly because of this heavy olfactory input. A sparser olfactory projection is also present to the areas identified as the medial and dorsal pallia as well. In lampreys, a nuclear area homologous to the amygdala of other vertebrates has not yet been identified. A cell-poor area bordering the striatum may be a candidate for an amygdalar homologue, however, because olfactory fibers terminate there.

In squalomorph sharks (Fig. 29-3), the olfactory bulbs are covered by a layer of olfactory nerve fibers, deep to which are a **glomerular layer** and an **internal cellular layer**. The latter layer contains both mitral and granular cells. The layers of the olfactory peduncle can be traced into a **medial** as well as a **lateral pallial area**, which are thus interpreted as subdivisions of the lateral pallium in receipt of olfactory projections. A nucleus (called **nucleus A** in some cases and **nucleus X** or **nucleus N** in others) in the lateroventral part of the telencephalon may be homologous to the cortical, olfactory-recipient amygdala of other vertebrates. This nucleus receives projections from the olfactory bulb.

In nonteleost ray-finned fishes, the olfactory bulbs (Fig. 29-4) are covered by an outer layer of olfactory nerve fibers over the **glomerular layer**. Deep to the glomerular layer is an **external cellular layer** that contains both mitral cells and smaller, **periglomerular cells**. The axons of the periglomerular cells project peripherally to the receptor cells in the olfactory epithelium. A layer primarily of **secondary olfactory**

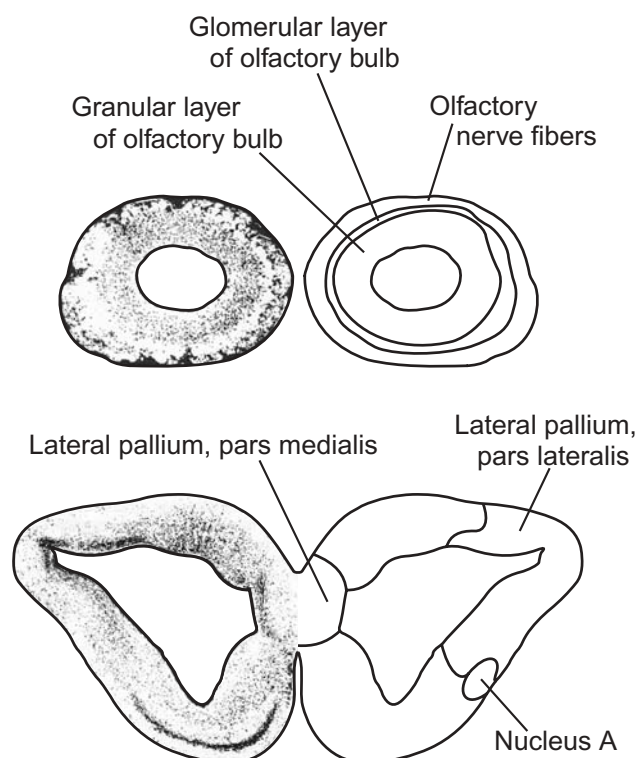


FIGURE 29-3. Transverse hemisections with mirror-image drawings through the olfactory bulb (top) and telencephalon of a squalomorph shark (*Squalus acanthias*). Adapted from Northcutt et al. (1988) and used with permission of John Wiley & Sons.

fibers lies deep to the external cellular layer. This layer is primarily composed of the axons of mitral cells and divides into the medial and lateral olfactory tracts. The deepest layer of neurons is the **internal cellular layer** and contains granule cells. A caudally lying nucleus, called the **supracommissural nucleus of the ventral telencephalic area (Vs)**, receives olfactory projections via the medial olfactory tract and has been identified as an amygdalar structure.

Due to the development of the telencephalon by eversion instead of evagination, the most medial pallial field, sometimes designated P1, or the **dorsomedial pallium** (Fig. 29-4), is the major site of termination of olfactory bulb projections in cladistians. The olfactory fibers terminate on the more distal parts of the dendrites of the pallial cells, which lie in a periventricular position. This pallial area is thought to be homologous to the lateral, olfactory pallium of vertebrates with evaginated telencephalic hemispheres. The olfactory bulb also projects, although through many fewer fibers, to the more distal part of the pallium, now called the **dorsolateral pallium** (see Chapters 19 and 25). Likewise, in sturgeons, olfactory bulb projections are heavy to the dorsomedial part of the pallium and light to the more distally lying dorsolateral part of the pallium. In some fishes, including sturgeons and some teleosts, primary olfactory projections that arise from the olfactory epithelium have been studied as well. Of course, the olfactory epithelium projects massively to the olfactory bulb, the axons of the epithelial cells forming the olfactory nerve, but these cells also project to central targets. Their projections generally are to the same sites as those that arise from the olfactory bulb.

In the coelacanth *Latimeria*, the olfactory bulb is covered by olfactory nerve fibers and contains a glomerular layer, a cellular zone that is presumed to contain mitral cells, and a more internal zone of granular cells. During the development of the telencephalon in *Latimeria*, the ventral, subpallial part evaginates. The dorsal, pallial part does not undergo an evagination, however, but is thickened and similar to the everted, pallial part of the telencephalon in ray-finned fishes. The olfactory tract lies in a central position within the pallial part of the telencephalon (Fig. 29-5).

In lungfishes, the olfactory bulbs contain a superficial olfactory nerve layer, a **glomerular layer**, an **external plexiform layer** of fibers, a **mitral cell layer**, an **internal plexiform layer**, and an **internal granular cell layer**. The transition zone between the olfactory bulb and the pallium is marked by a loss of the glomerular layer. Olfactory fibers project to areas identified, on topological, cytoarchitectonic, and histochemical grounds, as both the lateral and dorsal pallia. An area that lies ventral to the septal area and in the caudal part of the telencephalon, called the **central subpallium**, is present and may be homologous to part or all of the amygdala of other vertebrates.

In some tetrapods, both a main olfactory bulb (in receipt of olfactory nerve fibers) and an accessory olfactory bulb (in receipt of vomeronasal nerve fibers) are present. In amphibians the main olfactory bulb (Figs. 29-6 and 29-7) comprises a superficial layer of olfactory afferent fibers (rostral to the level shown in Fig. 29-7), a **glomerular layer**, an **external plexiform layer**, a **mitral cell layer**, and an **internal granular cell layer**. As is also the case in lungfishes, the granular cell layer is relatively thick and densely packed with cells. In amphibians, mitral cell axons enter the lateral olfactory tract (not shown in Fig. 29-7) and terminate in the **lateral pallium** and the ventral half of the dorsal pallium. In frogs, some fibers from the medial olfactory tract reach part of the rostral medial pallium, and in salamanders, some medial olfactory tract fibers terminate in rostral parts of both the medial and dorsal pallia.

A number of connections of the lateral pallium, in addition to its input from the olfactory bulb, have been studied in amphibians. The lateral pallium also receives afferent projections from the medial pallium and from the septum, amygdala, entopeduncular nucleus, preoptic area, anterior and central parts of the dorsal thalamus, and infundibular hypothalamus. Thus, the olfactory processing done by the lateral pallium is modulated by a number of forebrain inputs. The output of the lateral pallium in amphibians is predominantly within the telencephalon—to the olfactory bulb, medial pallium, dorsal pallium, diagonal band, septum, and striatum. Although the lateral pallium also projects directly to the infundibular hypothalamus, the main route by which the lateral pallium influences the hypothalamus is through the medial pallium.

Group II

Group II Anamniotes. In hagfishes, the olfactory nerves enter the olfactory bulb (Fig. 29-8) and terminate on the dendrites of mitral cells within the **glomerular layer**. A **periglomerular layer** and the **mitral cell layer** lie deep to the glomerular layer rostrally. In a more caudal part of the olfactory bulb, an **internal granular cell layer** is present. Both

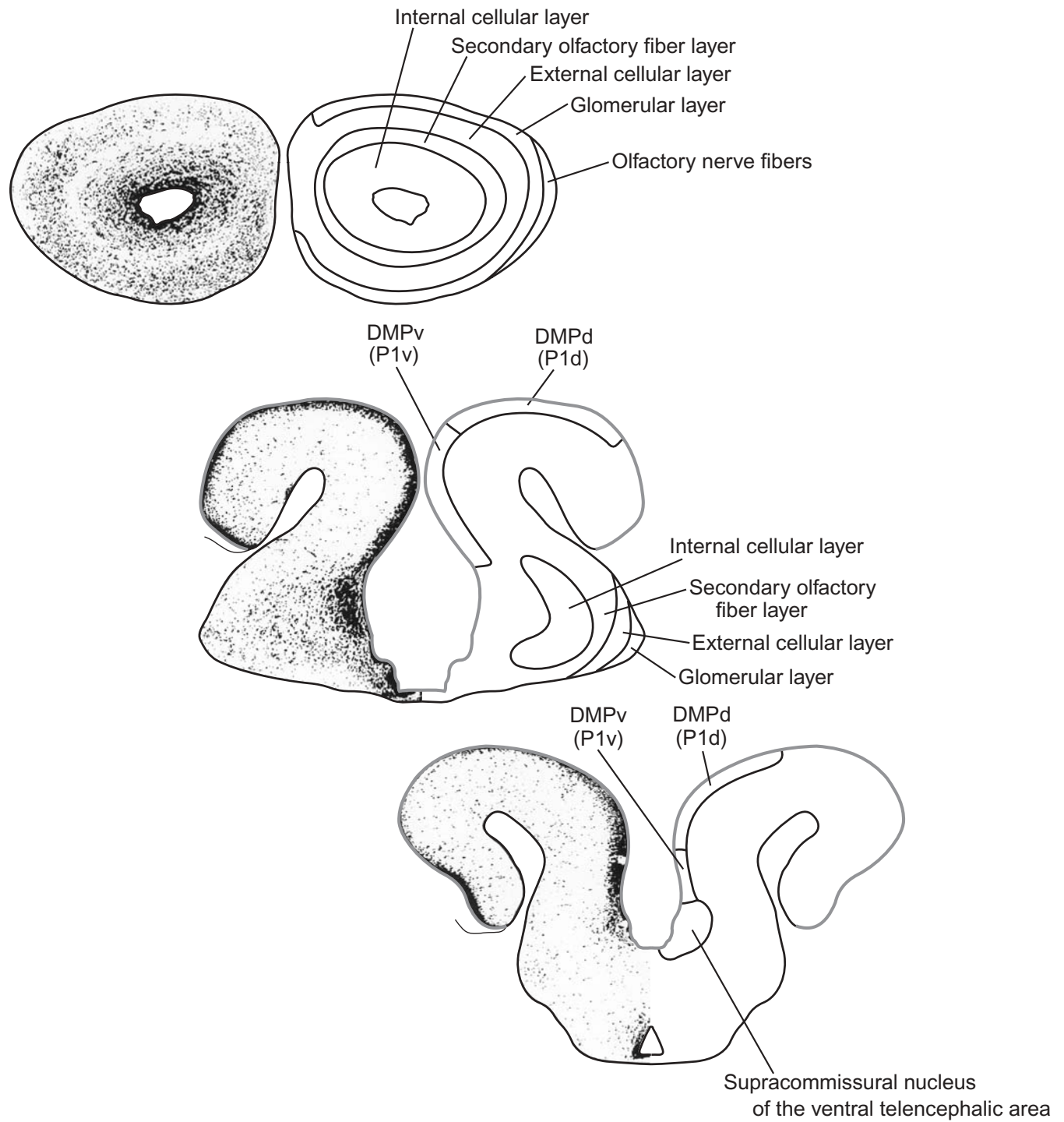


FIGURE 29-4. Transverse hemisections with mirror-image drawings through the olfactory bulb (top left), rostral telencephalon (middle), and caudal telencephalon (bottom right) of a bichir (*Polyterus palmas*). Adapted from Northcutt and Davis (1983) and used with permission of the University of Michigan Press. Abbreviations: DMPd, dorsal part of dorsomedial pallium; DMPv, ventral part of dorsomedial pallium.

mitral and granule cells contribute axons to the olfactory tract. No possible homologue of any amygdalar division has been identified in hagfishes.

The pallium of the telencephalon in hagfishes can be divided into five major divisions, three of which are shown in Figure 29-8, and the lateral olfactory tract projects massively to all five divisions. The lateral olfactory tract forms deep and superficial divisions that course within the deepest (P5) and the most superficial (P1) pallial divisions, respectively. The deep division of the lateral olfactory tract is unique to

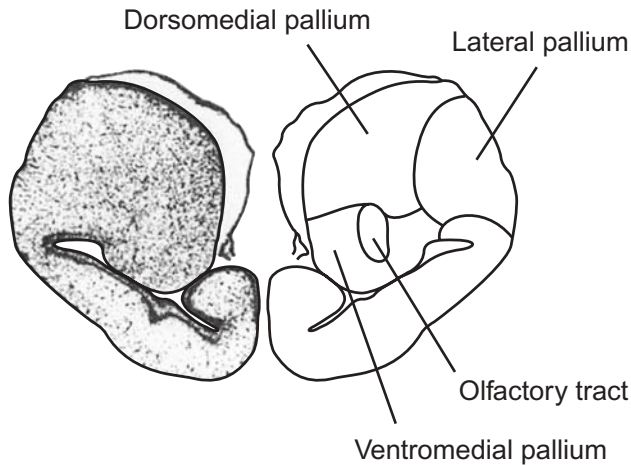


FIGURE 29-5. Transverse hemisection with mirror-image drawing through the telencephalon of the coelacanth (*Latimeria chalumnae*). Adapted from Northcutt (1995) and used with permission of S Karger AG, Basel. Terminology and areal anatomy is based on Nieuwenhuys and Meek (1990b).

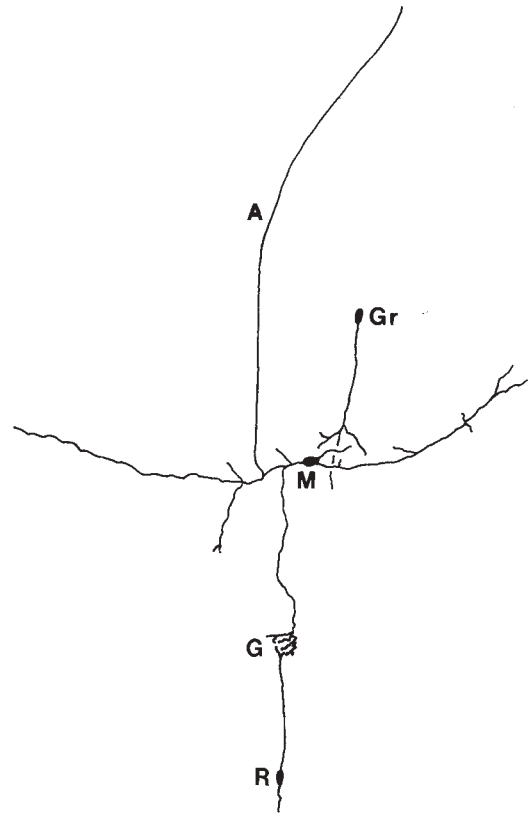


FIGURE 29-6. Drawing of a mitral cell (M) in the olfactory bulb of a frog (*Rana pipiens*) as seen in a Golgi preparation. An olfactory receptor cell (R) synapses on a glomerulus (G) on the distal end of a mitral cell dendrite. A granule cell (Gr) also synapses on the mitral cell. The axon (A) of the mitral cell projects to olfactory cortex. Adapted from Scalia et al. (1991) and used with permission of John Wiley & Sons.

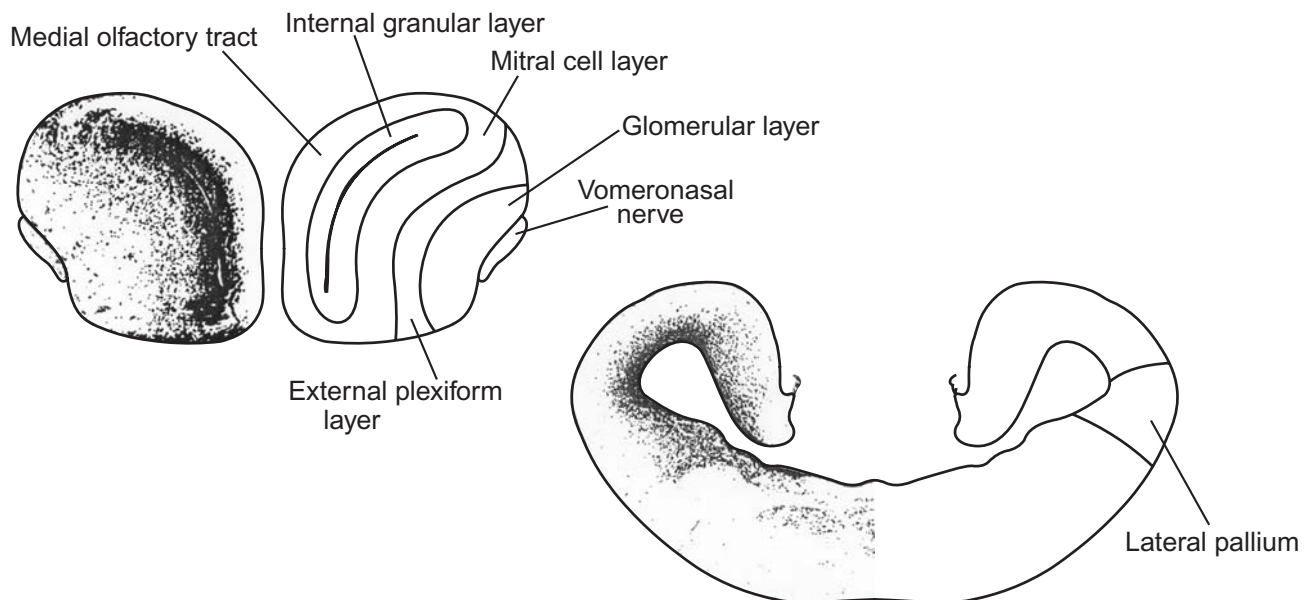


FIGURE 29-7. Transverse hemisections with mirror-image drawings through the olfactory bulb (top) and telencephalon of a tiger salamander (*Ambystoma tigrinum*). Adapted from Northcutt and Kicliter (1980) and used with kind permission of Springer Science and Business Media.

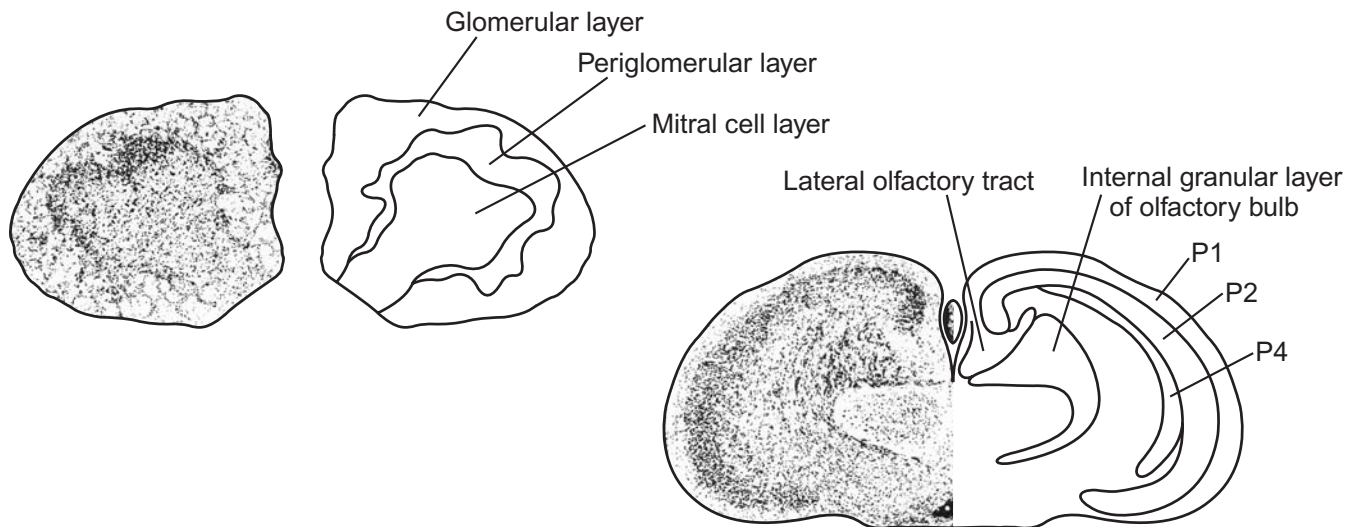


FIGURE 29-8. Transverse hemisections with mirror-image drawings through the olfactory bulb (left) and telencephalon of a hagfish (*Eptatretus stouti*). P1, P2, and P4 are pallial areas. Adapted from Wicht and Northcutt (1992) and used with permission of S Karger AG, Basel.

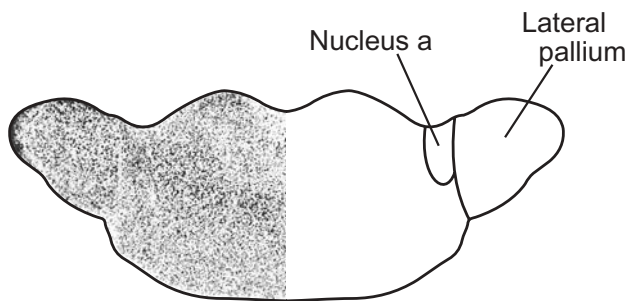


FIGURE 29-9. Transverse hemisection with mirror-image drawing through the telencephalon of a skate (*Raja eglanteria*). Adapted from Northcutt (1978).

hagfishes. Whether the entire pallium in hagfishes is homologous to the lateral, piriform pallium of other vertebrates or is a field homologue of two or more of the pallial areas present in other vertebrates is an unresolved question. Studies of the efferent projections of the various divisions of the pallium and of other afferent projections may help to clarify telencephalic organization in these animals.

In Group II cartilaginous fishes, the olfactory bulb is superficially covered by a layer of olfactory receptor cell axons and contains **glomerular**, **mitral**, and **granular cell layers**. Fibers from the olfactory bulb divide into lateral and medial olfactory tracts in Group II sharks and terminate in the dorsal and lateral pallia. In skates (Fig. 29-9), only a single olfactory tract can be distinguished. This tract terminates in the lateral pallium and may also innervate a region on the medial border of the lateral pallium called **nucleus a**. A good candidate for an olfactory-recipient amygdalar homologue has not yet been identified in any Group II cartilaginous fish, however.

In teleosts, the olfactory nerve fibers form a superficial layer over the olfactory bulb. The olfactory bulb [Fig. 29-10(A, B)]

contains **glomerular**, **mitral**, **secondary olfactory fiber**, and **internal granular cell layers**. An example of a mitral cell in a carp is shown in Figure 29-11, although the morphology varies to some extent. A second type of neuron is present in the mitral cell layer in at least some teleosts and is called a **ruffed cell** in reference to the presence of many pedunculated protrusions on the initial portion of the axon. The axons of ruffed cells are believed to project into the telencephalon along with the mitral cell axons. The ruffed cells are unusual neurons, however, in that their dendrites surround the dendrites of the mitral cells like glial processes, rather than receiving an array of synaptic inputs, while the ruffed portion of their axons have reciprocal synapses with granule cells. Their function in olfactory processing and their evolutionary origin remain to be determined. The granular cells of teleosts have smooth dendrites; they lack axons and appear to play a major role in the integration of olfactory information within the olfactory bulb.

The olfactory tract in teleosts comprises medial and lateral divisions. The olfactory fibers terminate predominantly within the **posterior zone of area dorsalis telencephali, Dp** [Fig. 29-10(C, E)]. As in Type I ray-finned fishes, the olfactory bulb in teleosts also gives rise to minor projections to the more proximal part of the pallium, particularly to the more ventral part of the **medial zone of area dorsalis telencephali, Dm**. Recently, evidence of direct projections from the olfactory receptor cells to the posterior zone of area dorsalis and to the ventral and commissural nuclei of area ventralis (see Fig. 30-8) has also been found. Receptor cell axons that bypass the glomeruli of the mitral cells and continue to the telencephalon along with the axons of the mitral cells account for these projections.

In teleosts, five caudally situated areas—**NT (nucleus taenia)** and **Vs, Vp, Vc, and Vi**—the **supracommissural**, **postcommissural**, **commissural**, and **intermediate nuclei of area ventralis**, respectively [Fig. 29-10(D, E)], receive projections from the olfactory bulb and are considered to be

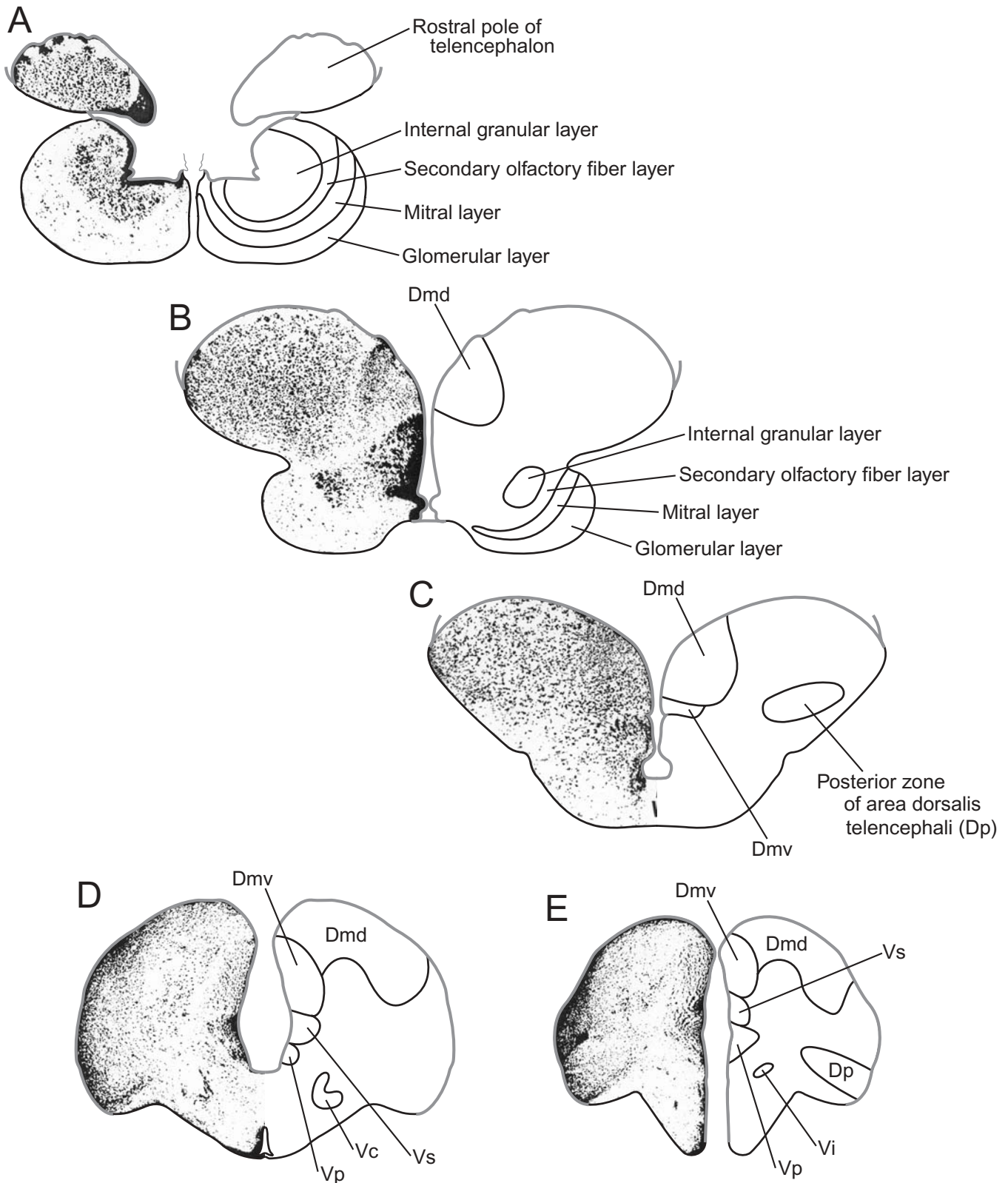


FIGURE 29-10. Transverse hemisections with mirror-image drawings through the olfactory bulb and rostral telencephalon in the teleost *Salmo gairdneri* (A–C) to best show these structures and through the caudal telencephalon in the euteleost *Lepomis cyanellus* (D–E) to best show the nuclei in area ventralis. Abbreviations: Dmd, dorsal part of Dm, the medial zone of area dorsalis; Dmv, ventral part of Dm; Vc, commissural nucleus of area ventralis (V); Vd, dorsal nucleus of V; Vi, intermediate nucleus of V; Vp, postcommissural nucleus of V; Vs, supracommissural nucleus of V. Nucleus taenia (NT) is not present at these levels. Adapted from Northcutt and Davis (1983) and used with permission of the University of Michigan Press.

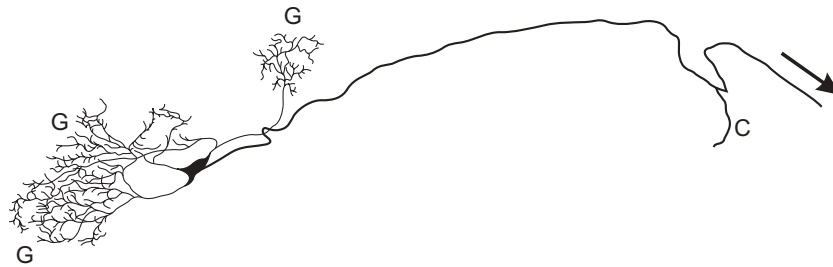


FIGURE 29-11. Drawing of a mitral cell as reconstructed from a Golgi preparation in the olfactory bulb of a carp. The distal part of the mitral cell dendrite ramifies to form several glomerular tufts (G). The axon gives off a collateral branch (C) before continuing into the telencephalon (arrow). Data from Satou (1990).

homologous to olfactory-recipient parts of the amygdala of other vertebrates. Vc also has been proposed as a striatal component, so a homology with the olfactory striatal amygdala of amniotes is possible—specifically the medial nucleus of the amygdala of mammals.

Amniotes. The olfactory system has been studied in most detail in mammals. The neuronal organization of the mammalian olfactory bulb is shown semi-schematically in Figure 29-12. The chemosensory receptor cells terminate on mitral cell dendrites within the glomeruli in the **glomerular layer**. Centrifugal fibers, which arise in sites in the basal forebrain and project back to the olfactory bulb within the olfactory tract, synapse on the dendrites of granule cells, which, in turn, have reciprocal synapses with the mitral cell dendrites.

As in a variety of other vertebrates, the olfactory bulb in mammals gives rise to medial and lateral olfactory tracts. These tracts project to the **olfactory**, or **piriform**, **cortex**, which lies on the ventral surface of the telencephalon, and to neighboring areas including an **anterior olfactory nucleus** and the **olfactory tubercle**. These latter structures (particularly the anterior olfactory nucleus) are sometimes considered to be parts of the olfactory cortex itself, although the olfactory tubercle is now regarded, with nucleus accumbens, as the ventral striatum. The olfactory cortex projects to a variety of sites within the forebrain, including some neighboring neocortical areas, nucleus accumbens, parts of the amygdaloid complex, hippocampal formation, and the lateral part of the hypothalamus. The olfactory cortex also has a substantial efferent projection to a nucleus in the dorsal thalamus called the **mediodorsal nucleus**, which in turn relays olfactory information to the prefrontal cortex, as discussed in Chapter 25.

In addition to the sites listed above, the olfactory pallium in mammals comprises parts of the amygdala. The main olfactory bulb projects directly to several parts of the amygdala, including the anterior part and the lateral zone of the posterior part of the **cortical amygdalar nucleus**, best referred to by their abbreviations **COAa** and **COApI**, respectively. The main olfactory-recipient parts of the amygdala in turn project to other amygdalar nuclei, including a nonfrontotemporal part

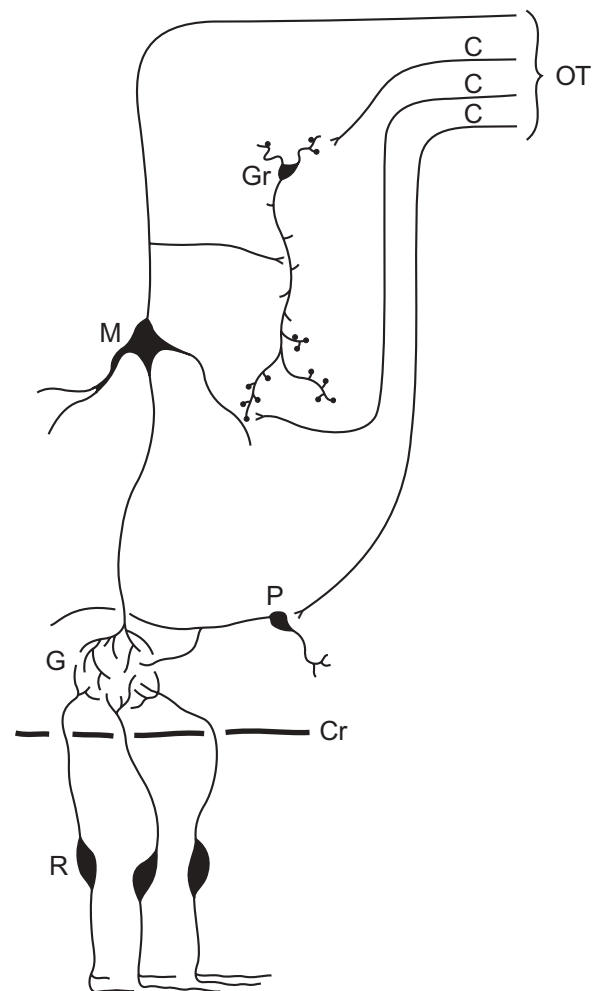


FIGURE 29-12. Schematic drawing of the organization of the olfactory bulb in mammals. Abbreviations: C: centrifugal fibers; Cr, cribriform plate; G, glomerulus; Gr, granule cell; M, mitral cell; OT, olfactory tract; P, periglomerular cell; R, receptor cell. Adapted from Heimer (1995, p. 271) and used with kind permission of Springer Science and Business Media.

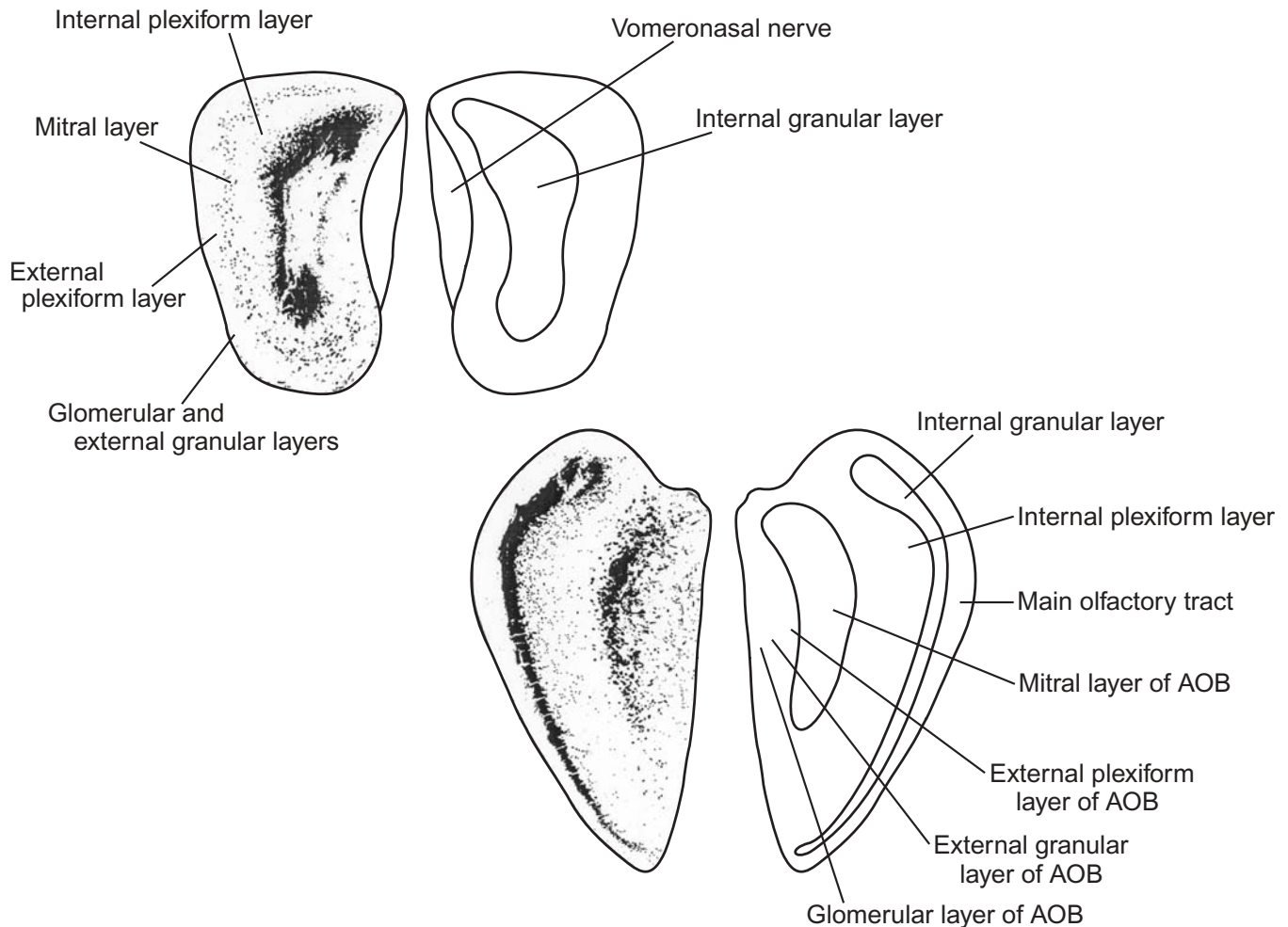


FIGURE 29-13. Transverse sections with mirror-image drawings through the main olfactory bulb (top) and the main and accessory olfactory bulbs in a snake (*Elaphe obsoleta rosalleni*). AOB = accessory olfactory bulb. Adapted from Halpern (1980) and used with kind permission of Springer Science and Business Media.

of the basolateral nucleus (its posterior part), the basomedial nucleus, and the posterior amygdalar nucleus, most of which then project to the medial part of the hypothalamus. Additionally, olfactory-related pallial amygdalar components project to the subpallial central and medial amygdalar nuclei. Thus, the olfactory inputs to the cortical and related parts of the amygdala are relayed through other amygdalar nuclei to the hypothalamus and to the amygdalar striatum.

In reptiles (Fig. 29-13), the main olfactory bulb is covered by olfactory nerve fibers and contains a **glomerular layer** of glomeruli and periglomerular cells, an **external granular layer** of small cells, an **external plexiform layer** with a few displaced mitral cells, a **mitral cell layer**, an **internal plexiform layer**, and a densely packed **internal granular layer**. The olfactory tract projects to the **lateral**, or **piriform**, **cortex** in the lateral part of the telencephalic pallium, as shown in a lizard in Figure 29-14. The olfactory bulbs of birds (Fig. 29-15) are organized in a like manner and project to lateral, or piriform cortex. Efferent projections of the lateral cortex have

been studied to some extent in reptiles and birds; lateral cortical efferents to nucleus dorsomedialis in the dorsal thalamus of birds recently have been described.

Amygdalar components also receive direct projections from the main olfactory bulb in reptiles. Two parts of the more caudal part of the DVR region, called the **ventral anterior amygdala** and the **external amygdala**, have been identified as good candidates for a homologue of the cortical amygdala of mammals. As in mammals, these nuclei project to another putative amygdalar component, the PDVR, which in turn projects to the hypothalamus. In birds, the main olfactory system is minor compared with other sensory systems; thus, comparable amygdalar cell groups have not yet been identified.

VOMERONASAL SYSTEM

A vomeronasal nerve occurs only in tetrapods. It is present in amphibians and, among amniotes, in mammals and most

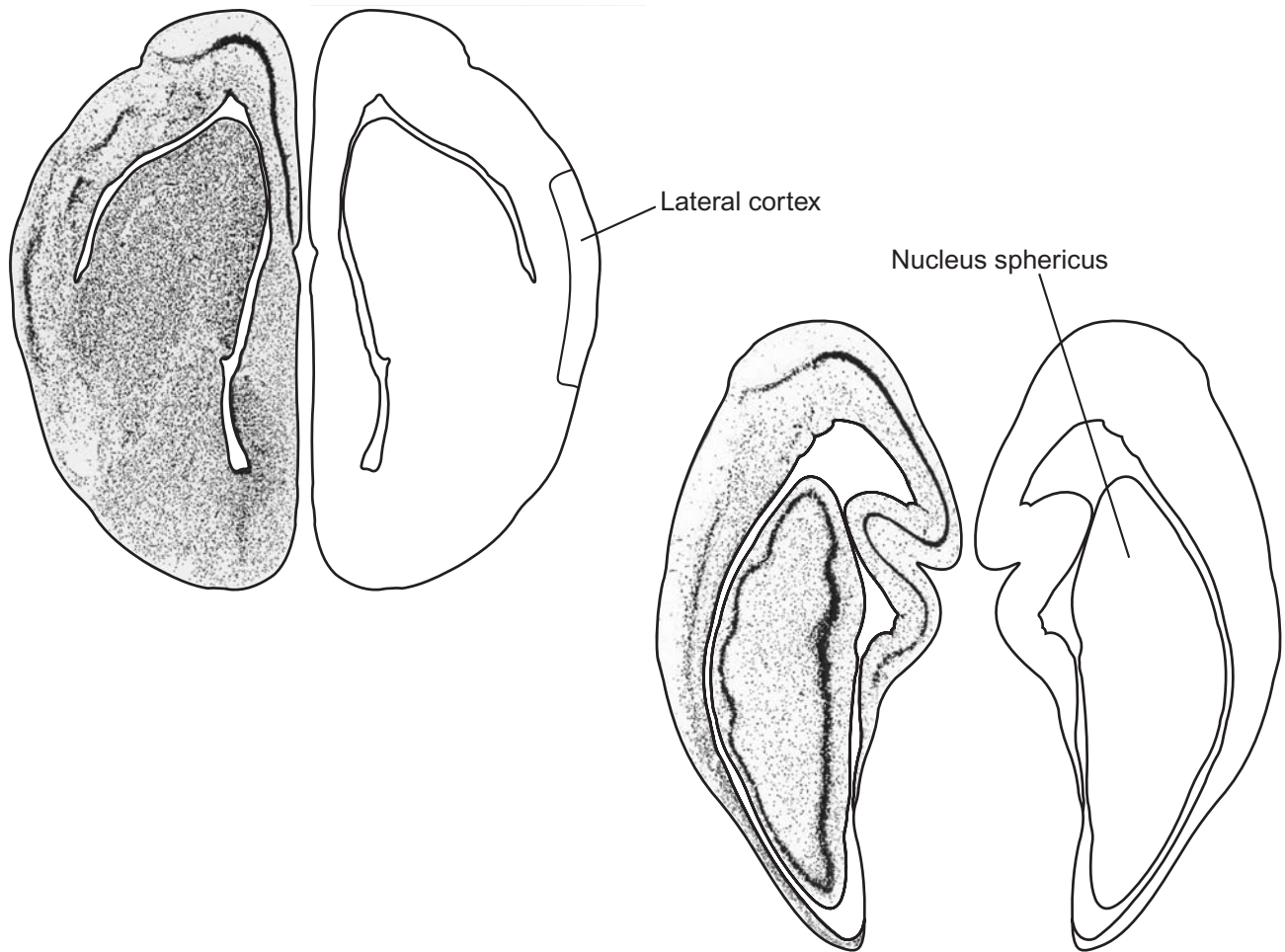


FIGURE 29-14. Transverse sections with mirror-image drawings through the telencephalon of a lizard (*Tupinambis nigropunctatus*). The upper section is more rostral. Adapted from Ebbesson and Voneida (1969) and used with permission of S Karger AG, Basel.

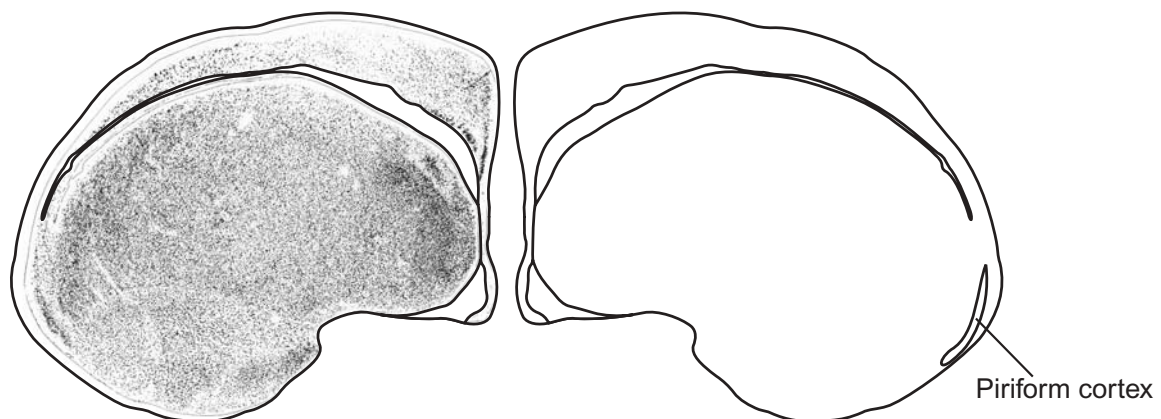


FIGURE 29-15. Transverse hemisection with mirror-image drawing through the telencephalon of a bird (*Columba livia*). Adapted from Karten and Hodos (1967) and used with permission of The Johns Hopkins University Press.

squamate reptiles (lizards and snakes). It is absent in the thecodonts (crocodiles and birds) and in turtles. Whether it is present in the rhynchocephalian *Sphenodon* is unclear. Until recently, this nerve was believed to be absent in some mammals, including some of the primates, but recent evidence suggests that it is probably present in all mammals. The nerve has bipolar cells with dendrites ending in the olfactory epithelium, either in a restricted part of the olfactory epithelial area, as in urodele amphibians, or in a blind pouch next to the epithelial surface and called the **vomerolateral** (or **Jacobson's organ**), as in other amphibians and amniotes. The vomeronasal nerve projects to the accessory olfactory bulb.

In amphibians, the accessory olfactory bulb is present as a thickened part of the caudal wall of the main olfactory bulb. Neurons in the accessory olfactory bulb project to the ventrolateral tip of the lateral pallium, an area that is called the lateral prominence and may in fact be a part of the amygdala rather than of the lateral pallium. The accessory olfactory bulb projects most heavily to a more ventral part of the forebrain, now called the **medial amygdala** (formerly called the pars lateralis of the amygdala) (Fig. 29-16). As discussed in Chapter 24, this is a subpallial nucleus that appears to be homologous to the medial amygdaloid nucleus of mammals.

Among mammals, the vomeronasal system is well developed in several orders, including rodents. Within the pallium,

the accessory olfactory bulb projects to the lateral zone of the posterior part of the cortical amygdala, **COApl**. It also projects directly to the subpallial **medial amygdaloid nucleus**. Both the latter and COApl are reciprocally interconnected with another pallial amygdalar component, the posterior amygdaloid nucleus. The main output from the vomeronasal-related amygdala is from the medial and posterior nuclei to the medial part of the hypothalamus.

In lizards and snakes, in which both olfactory and vomeronasal systems are present, the accessory olfactory bulb projects to a nucleus in the caudal part of the dorsal ventricular ridge called **nucleus sphericus** (Fig. 29-14). Nucleus sphericus is a distinctive nucleus in the caudal part of the amygdalar region that is formed by an oval lamina of cells (as seen in transverse section). The neurons of nucleus sphericus concentrate sex hormones, as do some of the other amygdaloid nuclei. This nucleus projects to several sites where vomeronasal and main olfactory inputs converge, including part of the lateral cortex and the ventral anterior and external amygdalar nuclei. As in other amniotes, the accessory olfactory bulb also projects to the subpallial medial amygdala. The vomeronasal system plays an important role in mediating unconditioned and reinforcing properties of natural chemicals, such as those used for prey trailing by snakes, as discussed in Box 29-1. In mammals, the pheromonal cues detected by the vomeronasal system are

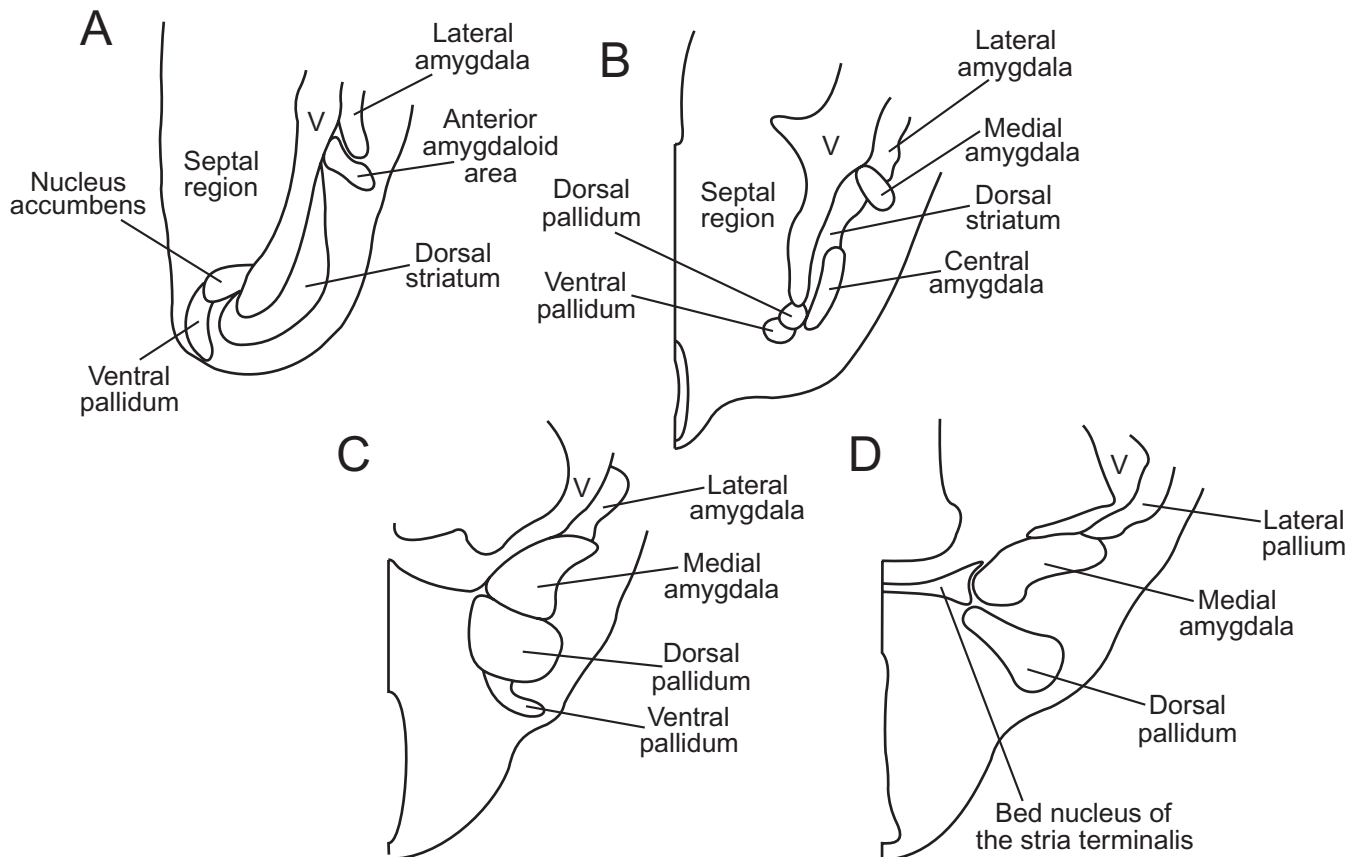


FIGURE 29-16. Series of drawings in rostral (A) to caudal (D) order of the ventral part of the hemisphere on the right side in a bullfrog (*Rana perezi*). Striatopallidal components and other landmarks are included for orientation. Adapted from Marín et al. (1998) and used with permission of John Wiley & Sons.

BOX 29-I. The Olfactory and Vomeronasal Systems of Snakes

Mimi Halpern, Alino Martínez-Marcos, Enrique Lanuza, and their co-workers have carried out extensive studies of the olfactory and vomeronasal systems in the garter snake, *Thamnophis sirtalis*. Garter snakes use tongue-flicking of the substrate to sample chemical stimuli on it. The molecules picked up by the forked tongue are conveyed to the vomeronasal system. This system is used to follow odorant trails on the substrate, and it also functions during prey ingestion, contributing to its reinforcing value. In contrast, airborne molecules, which are usually of lighter weight, are sampled by the main olfactory system. This system appears to function as the initial alerting system for the detection of airborne prey odors and is then used by the snake to follow the odor stream to locate the prey.

The intratelencephalic connections of the main and vomeronasal (accessory) olfactory systems involve a number of structures. The main olfactory bulb projects to the full extent of the lateral cortex. The accessory olfactory bulb projects to nucleus sphericus, which in turn projects to several targets, including the rostroventral part of the lateral cortex. This part of the lateral cortex contains many double-pyramidal cells, which are in a position to receive main olfactory inputs on the externally directed dendritic tree and the vomeronasal-sphericus relayed inputs on the internally directed branches. This synaptology needs to be confirmed with further experiments but is suggested by the patterns of termination of the different inputs relative to the neuronal geometry. Most or all of these double-pyramidal neurons project to the medial cortex, which in turn projects to the septal region.

A descending pathway through the hypothalamus to the hypoglossal nucleus has also been identified, which provides the neural basis for tongue-flicking responses. Tongue-flicking occurs both for sampling the substrate for the vomeronasal system and in the presence of airborne odorants. In addition to projecting to the rostroventral part of lateral cortex and giving rise to a very minor direct projection to the hypothalamus, nucleus sphericus also projects to a rostral part of the striatal region called the **olfactostriatum**, which lies at rostral telencephalic levels between the olfactory tubercle ventrally and nucleus accumbens dorsally. The olfactostriatum projects to a variety of targets, including the septal region, lateral cortex, some amygdaloid nuclei, ventral pallidum, and hypothalamus. Among its amygdalar targets is the **medial amygdala**, which also receives vomeronasal inputs directly from the accessory olfactory bulb and from nucleus sphericus as well as both main olfactory and vomeronasal inputs from the rostroventral part of the lateral cortex. Thus, the medial amygdala

receives both main olfactory and vomeronasal inputs, and its main projection is to the **lateral posterior nucleus** of the hypothalamus. This hypothalamic nucleus in turn projects caudally to the hypoglossal nucleus, which innervates the muscles of the tongue.

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essential for some components of normal copulatory behavior and affect the regulation of the onset of puberty, female cyclicity, the release of some hormones, the maintenance of pregnancy, maternal behavior, and other related functions.

TERMINAL NERVE

The function of the terminal nerve is uncertain, although it is currently suspected of having a neuromodulatory role, regulating neuronal excitability in the various sites to which it projects, including areas within the more ventral and medial parts of the forebrain. The nerve has been found to project to the retina and to the optic tectum in teleost fishes. It was described in cartilaginous fishes by Fritsch in 1878 and by Locy in 1905 and is now known to be widely distributed among vertebrates. The dendrites of terminal nerve neurons are distributed on the nasal septum and are in close proximity to the blood vessels in that area. The cell bodies of these neurons are most frequently located within a nearby ganglion, but their position is variable, particularly within bony fishes.

The cell bodies of the terminal nerve contain **gonadotropin-releasing hormone (GnRH)**, which is sometimes alternatively called luteinizing hormone-releasing hormone (LHRH); these cell bodies are derived embryologically from neural crest. In mammals, most terminal nerve cell bodies lie in the ganglion of the nerve, but some additional GnRH-containing cells lie along the course of the nerve as it enters the brain. The GnRH-containing fibers of the terminal nerve project to the preoptic area, the medial part of the hypothalamus, the main and accessory olfactory bulbs, olfactory cortex, parts of neocortex, and the midbrain. A possible role for the terminal nerve in pheromonal responses for reproductive behavior, including the promotion of ejaculation by copulating males, has been suggested; however, the contribution of the terminal nerve in this and other behaviors, versus the contributions of the olfactory system, remains to be clarified. The central projections of the terminal nerve need further study in reptiles and birds, but they probably are to sites similar to those in mammals. The involvement of GnRH in various aspects of reproductive behavior has been established.

In lampreys, neurons that resemble the terminal nerve cell bodies of other vertebrates lie along the olfactory nerve as it enters the olfactory bulb, and the axons have been traced to the ventral thalamus, the ventral part of the hypothalamus, and the mesencephalic tegmentum. Unlike other vertebrates, however, terminal nerve fibers in lampreys do not appear to contain GnRH. In cartilaginous fishes, terminal nerve cell bodies are positive for GnRH and lie within as many as three ganglia as well as along the distal part of the nerve itself. The nerve appears to project mainly to the preoptic area and the septum; fibers also terminate directly on cerebral blood vessels. In sturgeons, a number of GnRH-positive cell bodies, presumably at least some of which are terminal nerve cell bodies, are distributed within the ventral part of the forebrain.

In lungfishes, the terminal nerve has two components: an anterior root (or **terminal nerve proper**) and a posterior root (also called the **nervus praepopticus**). Terminal/preoptic nerve fibers have been traced to the septum and to the preoptic

nucleus, but the terminal sites of more caudally passing fibers that enter the lateral forebrain bundle have yet to be identified. Terminal nerve projections to septal, preoptic, and hypothalamic sites have been found in amphibians, where, as in other vertebrates, GnRH appears to play a role in reproductive behaviors via the hypothalamic-pituitary system.

In teleost fishes, the terminal nerve cell bodies contain GnRH and project to medial, ventral sites in the forebrain. In teleosts in which the olfactory bulb is sessile, the majority of cell bodies of the terminal nerve do not lie in a ganglion but migrate into the medial and ventral parts of the forebrain. That intracerebral, GnRH-positive cells can originate from the neural crest and migrate into the forebrain has recently been confirmed with experimental embryological findings in zebrafish. In teleosts, the migrated terminal nerve neurons project to visual structures, particularly the retina. Diencephalic neurons that project to the retina also recently have been found in sturgeons, but whether these neurons are GnRH-positive terminal nerve neurons remains to be confirmed.

In teleosts, the migrated neurons of the terminal nerve form a broken rostrocaudal column through the ventral parts of the telencephalon and diencephalon. They have been referred to collectively as the **nucleus olfactorectinalis**. Axons from the cell bodies of the terminal nerve project to the retina via the optic nerve. In the retina, many of the fibers synapse on dopamine-containing **interplexiform cells**. The effect of the terminal nerve innervation of the retina on visual functions remains to be elucidated. A recent study of the terminal nerve ganglion in percomorph teleosts identified several sources of afferent projections to it, including a nucleus in the midbrain tegmentum called **nucleus tegmento-olfactorius**, which lies dorsal to a large nucleus called nucleus glomerulosus (see Chapter 20). This nucleus does not project to the olfactory bulb as its name implies but rather specifically and exclusively to the ganglion of the terminal nerve. It receives both visual and somatosensory inputs, as well as an input from the reticular formation, which it relays to the terminal nerve cells. The terminal nerve ganglion also receives inputs from several telencephalic sources, particularly the olfactory bulb itself and from olfactory bulb-recipient regions, the pars posterior of area dorsalis (Dp) and two parts of the area ventralis, Vs (pars supracommissuralis) and Vv (pars ventralis). Thus, these cells receive multisensory information—visual, somatosensory, and olfactory.

The terminal nerve in fishes is believed to play a role in reproductive behaviors due to the GnRH content of its neurons. The olfactory system may, however, play a more prominent role in reproduction. Exposure to sex pheromones has been found to increase the activity of olfactory nerve neurons in the medial part of the olfactory bulb but not of terminal nerve neurons. Tactile stimulation, on the other hand, was found to result in a decrease of terminal nerve neuron activity, and the contribution of the terminal nerve to reproductive behavior may thus be related to the physical contact that occurs during spawning behavior. Among the somatosensory inputs relayed to the ganglion of the terminal nerve in teleosts are those from the principal sensory nucleus of the trigeminal nerve, which thus may serve as a conduit for the effect of physical contact on the spawning behavior.

EVOLUTIONARY PERSPECTIVE

The olfactory nerve component of the rostral chemosensory system is present in all groups of vertebrates and is plesiomorphic for vertebrates. Olfactory projections to the pallium are restricted, mostly to the lateral pallium, in jawed vertebrates but are more extensive in lampreys and are to the entire pallium in hagfishes. From this distribution, extensive olfactory innervation of the pallium appears to be the plesiomorphic condition for vertebrates. Likewise, restricted pallial olfactory projections are the plesiomorphic condition for jawed vertebrates.

The presence of a terminal nerve in jawless vertebrates is questionable, but a terminal nerve is at least plesiomorphic for jawed vertebrates. In ray-finned fishes with sessile olfactory bulbs, the majority of cell bodies of the terminal nerve are in a migrated position within the brain. The projection of terminal nerve neurons to visual structures such as the retina is apomorphic in some or all ray-finned fishes. Although both olfactory and terminal nerve systems are present in most vertebrates, variation does occur. In toothed whales, for example, both the olfactory and vomeronasal systems have been lost, but the terminal nerve system has been markedly expanded.

The vomeronasal system is present in some tetrapods but not in nontetrapod vertebrates and is apomorphic for tetrapods. It has been secondarily lost in thecodonts (crocodiles and birds) and turtles and may also have been reduced or lost in *Sphenodon*. Although previously believed to be absent in some mammals; particularly primates, recent evidence suggests that a vomeronasal system may have been retained in all mammals.

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Limbic Telencephalon

INTRODUCTION

In most vertebrates, the medial part of the telencephalon comprises the telencephalic component of one of the brain's major coordinating systems, the limbic system. The main component of the telencephalic limbic system is the **medial pallium**, which contains the **hippocampal formation** and related pallial areas. The **septal nuclei** are an additional, mostly subpallial telencephalic component of the limbic system. Other structures outside the telencephalon also are considered to be part of the limbic system and include parts of the epithalamus, dorsal thalamus, and hypothalamus. In mammals, the major efferent tract from the hippocampal that distributes projections to the septal nuclei, hypothalamus, and other sites is called the **fornix**.

The amygdala is included in limbic system chapters in most textbooks. It is certainly highly interrelated with limbic structures in terms of its connections; however, as discussed in Chapter 19, it has four functionally distinct divisions, all of which are covered elsewhere in this book. The striatal components of the amygdala are covered in Chapter 24, the frontotemporal amygdala in Chapter 25, and the main and accessory olfactory amygdalae in Chapter 29. In this chapter, we will thus include mention of the amygdala and/or its various divisions as appropriate but will not focus on it specifically.

Generally speaking, in cartilaginous fishes and amphibians, both the dorsal and medial pallia receive sensory projections relayed from the rostral part of the dorsal thalamus, and the medial pallium receives the majority of these projections. Pallial homologies are still uncertain in ray-finned fishes, particularly for the distal pallium in cladistians; in Group II ray-finned fishes,

much of the pallium is sensory-recipient from projections relayed through the dorsal thalamus and additionally through the preglomerular nuclear complex and the inferior lobe of the hypothalamus. In teleosts, the putative homologue of the hippocampal formation of other vertebrate groups is located distally and is not in direct receipt of any known ascending sensory projection system. In amniotes, most of the retinal and somatosensory input to the diencephalon is relayed through the dorsal thalamus and to expanded, nonmedial parts of the pallium, with only a minor amount being relayed directly to the medial pallium. Pathways from these nonmedial pallial regions secondarily relay sensory information to the medial pallium. The rostral thalamic nuclei that relay a minor sensory input to the medial pallium are primarily involved in cortical-subcortical circuits with the medial pallium.

In mammals, behavioral studies indicate that the limbic system is involved in motivation, memory, learning, emotion, sexual behavior, and many integrative functions necessary for appropriate responses to stimuli. It plays a key role in spatial mapping for navigation through the environment and in many nonspatial tasks. The hippocampal formation is essential for short-term memory and is thus the gateway for the storage of new events in long-term memory. The limbic system also interacts with other major systems throughout the brain, particularly the olfactory system, other pallial areas, and the striatum. Both the septal nuclei and amygdala receive direct inputs from the olfactory bulb, while the hippocampal formation does not. The amygdala also is interconnected with the striatum, hypothalamus, and widespread areas of neocortex, including prefrontal cortex; its frontotemporal division relays inputs from the hippocampal formation to these sites either directly or through other amygdalar divisions.

Relatively few behavioral studies of these structures have been done in nonmammalian vertebrates. Those that have been done suggest that the telencephalic limbic structures play a similar role in these animals. Recent studies in fish are of particular interest in this regard, as highlighted below in Box 30-1.

THE LIMBIC PALLIUM IN ANAMNIOTES

Group I

In lampreys, a relatively small part of the telencephalon forms the medial pallium (Fig. 30-1). It receives inputs from a variety of structures, including the olfactory bulb, septal region and habenula, and various pallial and other diencephalic sites. It projects to multiple targets, including other parts of the pallium, olfactory bulb, and brainstem areas, such as thalamic and hypothalamic nuclei and the pretectum and optic tectum. In squalomorph sharks (Fig. 30-2), the medial pallium is also relatively small and is fused across the midline with the contralateral medial pallium. The medial pallium in squalomorph sharks is known to receive afferent projections from the dorsal pallium and the septal nucleus in the telencephalon and the posterior tubercle and a nucleus called the posterior lateral thalamic nucleus in the diencephalon. The latter nucleus relays input from the lateral line electrosensory system to the medial pallium.

In nonteleost ray-finned fishes (Fig. 30-3), the “medial” pallium lies in the distal (topologically lateral) part of the telencephalon, due to the development of the telencephalon by eversion (see Chapter 3). This pallial area previously has been referred to as the P3 part of the pallium, but more recent findings suggest that P3 and the more intermediate part of the pallium, P2, actually constitute a single, distal division called the **dorsolateral pallium** (Fig. 30-3). The part of the pallium previously called P3 is thus now called the lateral part of the dorsolateral pallium, or **DLPL**. Both parts of the dorsolateral pallium receive a sparse olfactory input, as well as a visual input

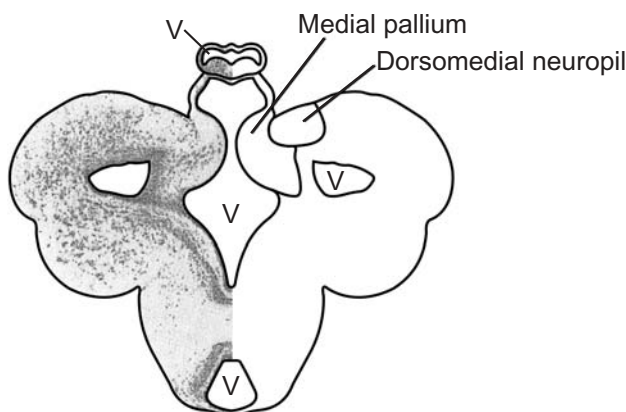


FIGURE 30-1. Transverse hemisection with mirror-image drawing through the telencephalon of a lamprey. Adapted from Northcutt and Wicht (1997) and used with permission of S Karger AG, Basel.

that is relayed from the optic tectum via a nucleus medianus, a component of the posterior tuberculum. The dorsolateral pallium does not receive any projections from dorsal thalamic nuclei, however.

In lungfishes (Fig. 30-4), **dorsal, intermediate, and ventral divisions** of the medial pallium can be identified on cytoarchitectural and histochemical grounds, but connections remain to be studied. In frogs (Fig. 30-5), the medial pallium is enlarged relative to its condition in lungfishes and to the dorsal and lateral pallia. It is possible to divide the medial pallium into three parts on cytoarchitectonic criteria, but these parts cannot be assumed to correspond one-to-one to the three parts of the medial pallium in lungfishes or to specific parts of the medial pallium in other vertebrates. Nonetheless, recent molecular findings on the pattern of expression of LIM-homeodomain genes strongly support homology of the medial pallium in frogs with the hippocampus of mammals. The medial pallium in frogs receives projections from the dorsal and lateral pallia, the nucleus of the diagonal band, the septal nuclei, the medial and lateral amygdalar nuclei, nucleus accumbens, and a bed nucleus of the pallial commissure. The latter nucleus is a small cell group in the medial part of the caudal telencephalon. The rostral part of the medial pallium also receives an input from the olfactory bulb. Afferent projections to the medial pallium from outside the telencephalon arise from the anterior nucleus of the dorsal thalamus, which relays somatosensory and other information, and from the serotonin-containing cells within the raphe division of the brainstem reticular formation.

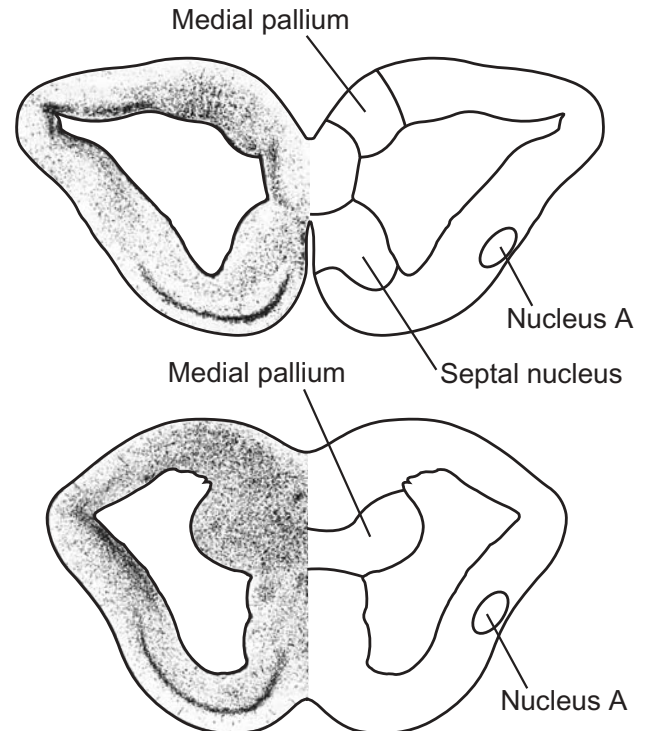


FIGURE 30-2. Transverse hemisections with mirror-image drawings through the telencephalon of a squalomorph shark (*Squalus acanthias*). The upper section is more rostral. Adapted from Northcutt et al. (1988) and used with permission of John Wiley & Sons.

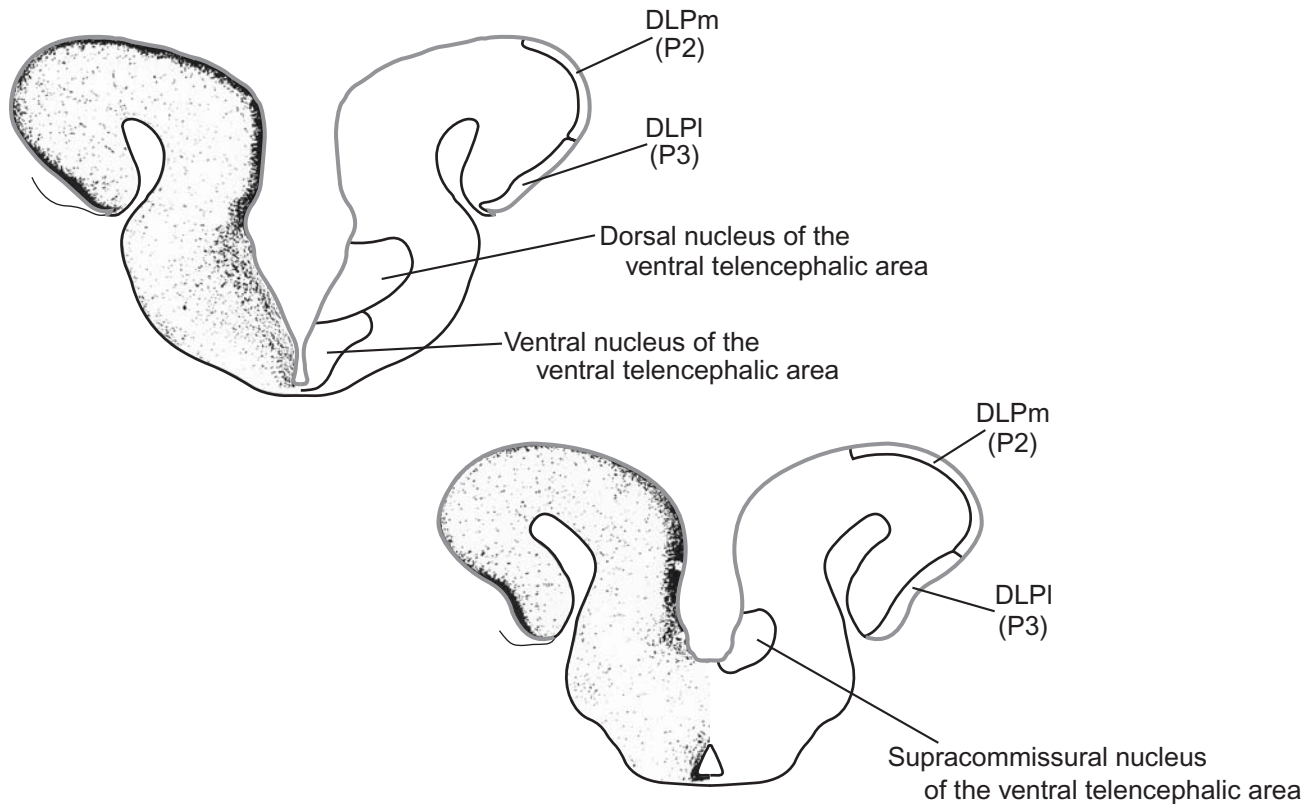


FIGURE 30-3. Transverse hemisections with mirror-image drawings through the telencephalon of a bichir (*Polypterus palmas*). The top section is more rostral. Abbreviations: DLPI, lateral part of dorsolateral pallium; DLPm, medial part of dorsolateral pallium. Adapted from Reiner and Northcutt (1992) and used with permission of John Wiley & Sons.

The medial pallium in frogs has reciprocal connections with the contralateral medial pallium. Within the telencephalon, it projects to a number of areas, including the septal nuclei, the bed nucleus of the pallial commissure, the diagonal band nucleus, the olfactory bulb, both parts of the amygdala, and the dorsal and lateral pallia. Outside the telencephalon it projects to structures including the habenula, nucleus anterior of the dorsal thalamus, ventral thalamus, preoptic area, and hypothalamus.

Group IIA

The telencephalon in hagfishes is large and complex (Fig. 30-6). The olfactory bulb is known to project to all parts of what appear to be pallial areas, whereas most portions of both the dorsal and medial pallia do not receive olfactory input in most vertebrates. Thalamic projections to the telencephalon have not yet been studied in hagfishes, so their distribution cannot yet be compared with the olfactory projections. Among galeomorph sharks, skates, and rays, the degree of elaboration of cell masses within the telencephalon varies from moderate to high. In skates (Fig. 30-7), the migration of cell masses in the telencephalon obscures relationships. A medial pallium has been identified in the dorsomedial telencephalon. Both electrosensory and visual inputs are known to reach the medial pallium in skates. Lateral line electrosensory input is relayed

through a caudal diencephalic nucleus, the lateral posterior thalamic nucleus, and visual input through nucleus anterior of the dorsal thalamus. The posterior tuberculum also projects to the medial pallium. Lateral line mechanosensory information also reaches the telencephalon, but the anatomy of this pathway is not yet known.

In both teleost and nonteleost ray-finned fishes, a pallial part of the telencephalon, called the area dorsalis, and a subpallial part, called the area ventralis, are present in the telencephalon (Fig. 30-8 and see also Fig. 25-5). Two parts of the pallium receive projections from the olfactory bulb—part of the medially lying **medial zone of area dorsalis, Dm**, and a region that lies in a caudal and lateral position called the **posterior zone of area dorsalis, Dp**. Whether secondary rearrangement of cell groups following the eversion process during development occurs is crucial for making accurate comparisons of these olfactory-recipient areas with pallial areas in other vertebrate taxa. Dp has been regarded by some as a migrated olfactory-receptive region that actually is part of Dm and continuous with it across the caudal pole of the telencephalon, as if torsion of the telencephalic wall occurred caudally, causing the displacement of this region. If this were the case, then Dp would be a component of the most proximal part of the pallium, comparable to the most lateral part of the pallium in taxa with evaginated pallia. Conversely, if it is not secondarily displaced in position, Dp may be a component of

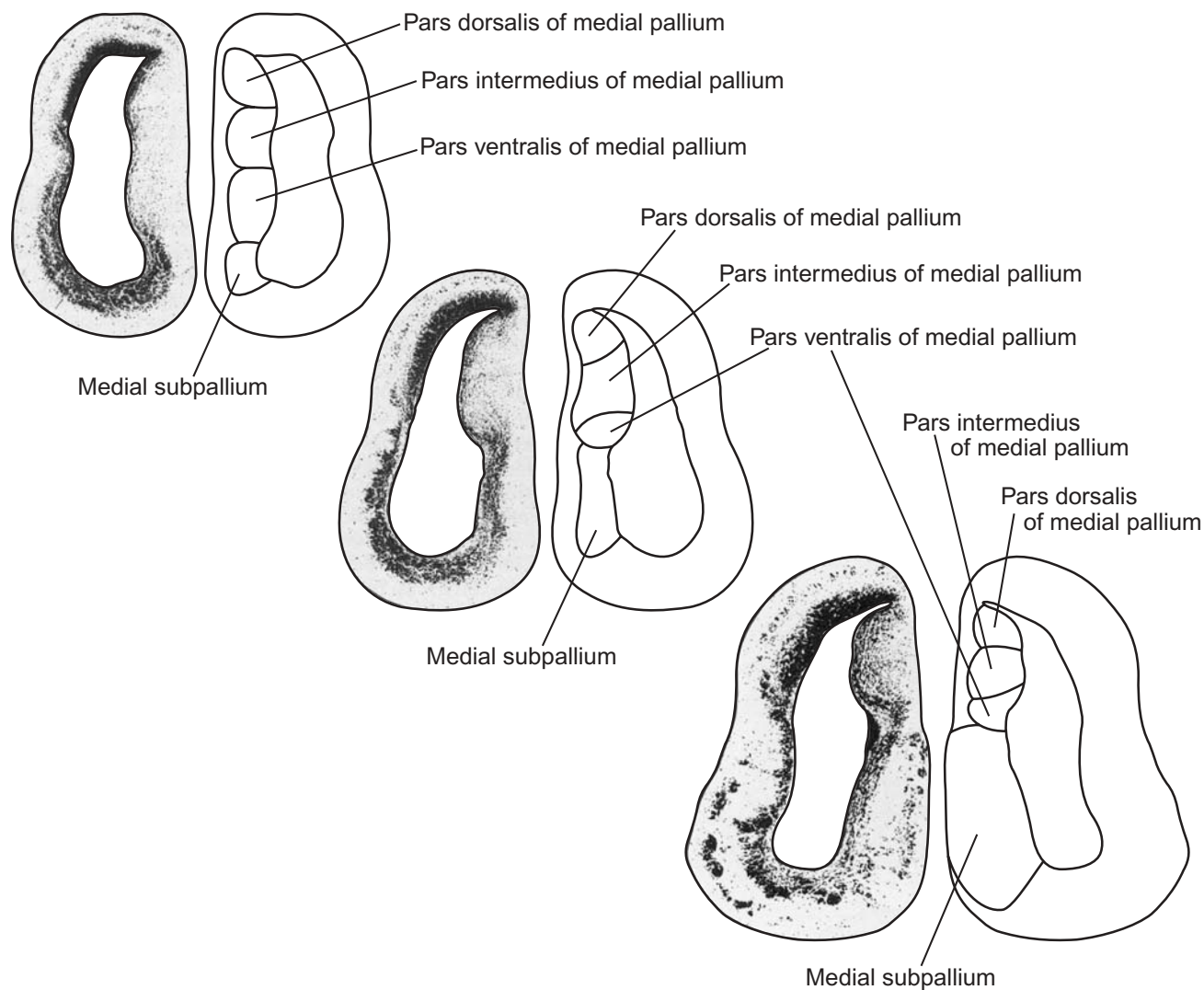


FIGURE 30-4. Transverse hemisections with mirror-image drawings through the telencephalon of a lungfish (*Protopterus annectens*). The top section is most rostral. Adapted from Reiner and Northcutt (1987) and used with permission of John Wiley & Sons.

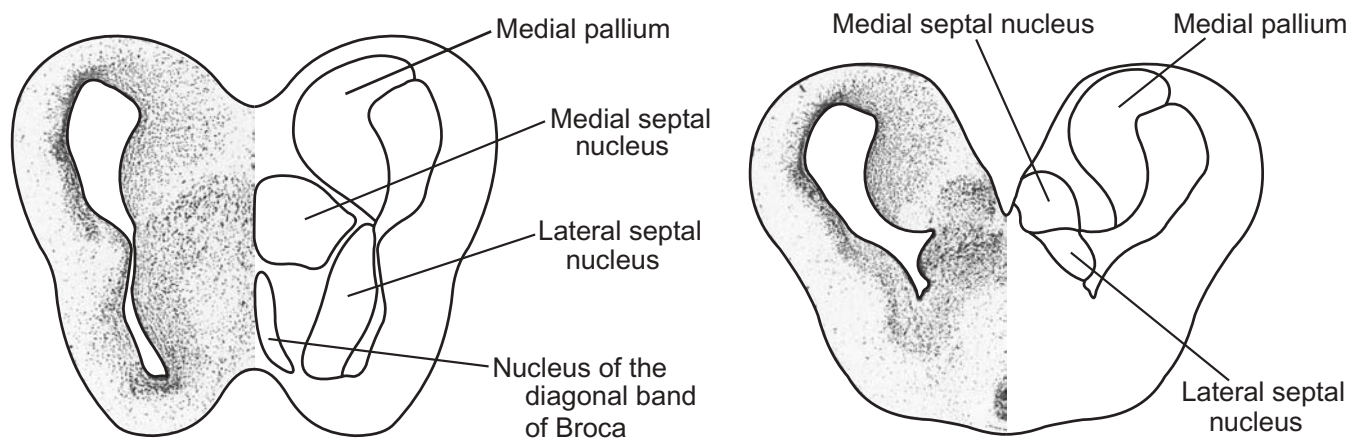


FIGURE 30-5. Transverse hemisections with mirror-image drawings through the telencephalon of a bullfrog (*Rana catesbeiana*). The section to the left is more rostral. Adapted from Wilczynski and Northcutt (1983) and used with permission of John Wiley & Sons.

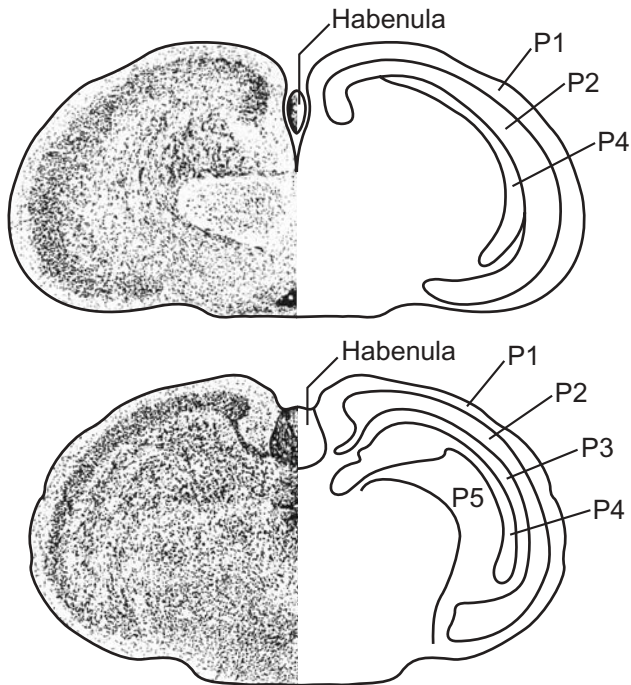


FIGURE 30-6. Transverse hemisections with mirror-image drawings through the telencephalon of a hagfish (*Eptatretus stouti*). The top section is more rostral. P1–P5 are pallial areas. Adapted from Wicht and Northcutt (1992) and used with permission of S Karger AG, Basel.

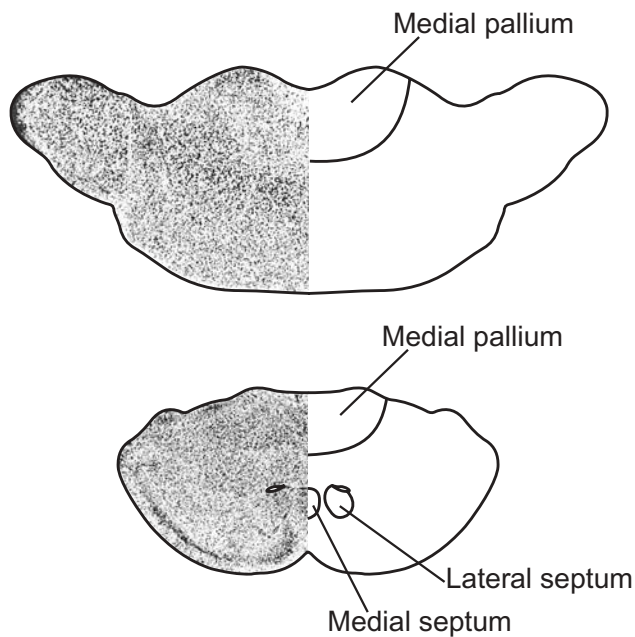


FIGURE 30-7. Transverse hemisections with mirror-image drawings through the telencephalon of a skate (*Raja eglanteria*). The top section is more rostral. Boundaries of cell groups based on Northcutt (1978).

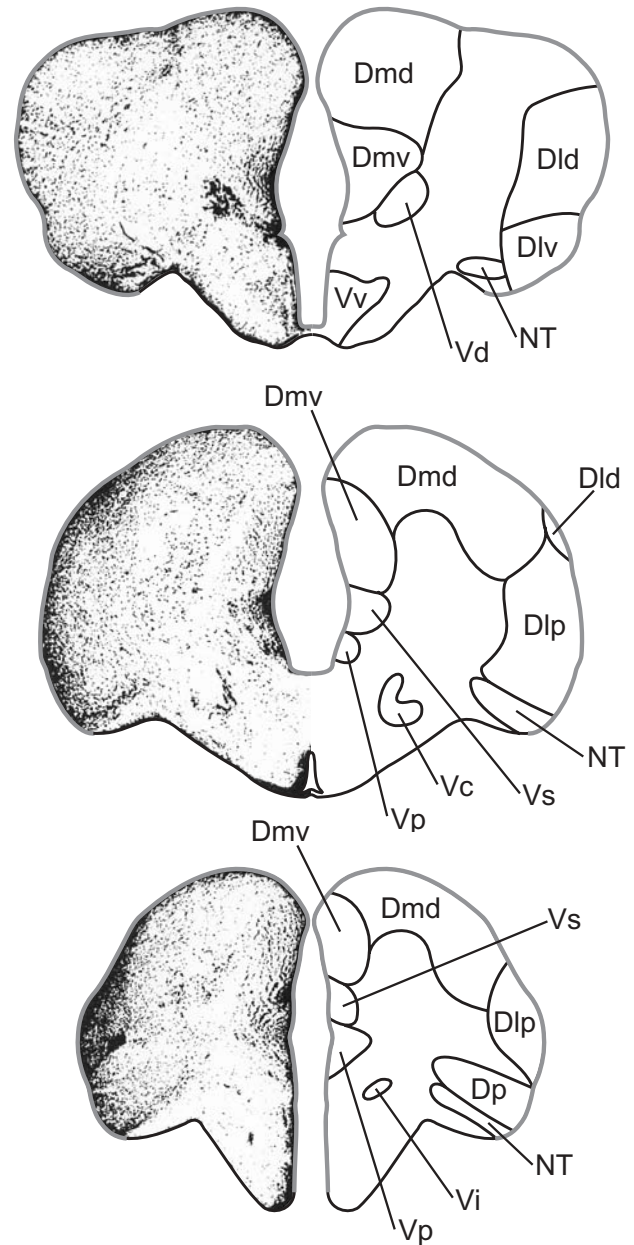


FIGURE 30-8. Transverse hemisections with mirror-image drawings through the telencephalon of a teleost (*Lepomis cyanellus*). The top section is most rostral. Abbreviations: Dld, dorsal part of lateral zone of area dorsalis (D); Dlp, posterior part of lateral zone of D; Dlv, ventral part of lateral zone of D; Dmd, dorsal part of medial zone of D; Dmv, ventral part of medial zone of D; Dp, posterior zone of D; NT, nucleus taenia; Vc, commissural nucleus of area ventralis (V); Vd, dorsal nucleus of V; Vi, intermediate nucleus of V; Vp, postcommissural nucleus of V; Vs, supra commissural nucleus of V; Vv, ventral nucleus of V. Adapted from Northcutt and Davis (1983) and used with permission of the University of Michigan Press.

the most distal part of the pallium. In this scenario, Dp would be an olfactory-recipient, distal pallial component that is juxtaposed and related to the hippocampal homologue (Dlv, as discussed below). Possible support for the latter arrangement is the finding in two ostariophysan fishes (the weakly electric

fish *Eigenmannia* and the zebrafish *Danio*) of a projection from Dp to the ventral nucleus of area ventralis, Vv, which, as discussed below, appears to be a septal nucleus. Whether this projection resembles that from the mammalian hippocampal formation to the septal nuclei via the fornix or from the amygdala via the stria terminalis is unresolved, however.

The hippocampus itself has been identified as lying within a part of the pallium immediately adjacent to Dp and referred to as the **lateral zone of area dorsalis (Dl)**, Figs. 30-8 and 25-5). Dl does not receive any direct projections from the olfactory bulb, and it lies in the distal part of the pallium, consistent with the simple eversion hypothesis. The ventral part of it, in particular, Dlv, is a very strong candidate for the hippocampus of fish, as discussed below in Box 30-1. A medially lying part of the pallium, the **medial zone of area dorsalis (Dm)**, previously was compared to part of the striatum of other vertebrates and has also been proposed as a homologue of the hippocampus. However, current evidence does not support

either of these comparisons. Dm is clearly part of the pallium, and recently, the ventral part of Dm, **Dmv**, has been found to receive a direct input from the olfactory bulb. This input is less substantial than the olfactory input to Dp but appears to be consistently present, particularly to the ventral part of Dm, across teleosts. Also, Dmv gives rise to projections to the hypothalamus that invite comparison with the amygdalohypothalamic pathways in other vertebrates. Specifically, on both connectional and positional grounds, Dmv is a strong candidate for the homologue of the olfactory part(s) of the amygdala in taxa with evaginated pallia. The more dorsal part of Dm, Dmd, may thus be the homologue of the frontotemporal amygdala. Both Dmd and Dl receive sensory inputs relayed through dorsal thalamic nuclei as well as through diencephalic nuclei outside the dorsal thalamus, that is, various parts of the preglomerular nuclear complex. These ascending sensory projections resemble the various collothamic projections to the frontotemporal amygdala in other vertebrate classes.

BOX 30-1. The Hippocampus and the Amygdala of Goldfish

Cosme Salas, Fernando Rodríguez, Cristina Broglio, and their co-workers in Seville, Spain, have carried out a series of experiments in goldfish that demonstrate hippocampal functions for the lateral, i.e., distal, part of the pallium, Dlv, and amygdalar functions for the medial part of the pallium, Dm—exactly where the hippocampus and the frontotemporal division of the amygdala, respectively, are predicted to lie from simple eversion of the telencephalic pallium without any secondary rearrangement.

Two different strategies can be used by animals to explore and navigate through the environment. One is an **egocentric** strategy, which involves guidance, the approaching or avoiding of objects, and orientation, which involves a body-centered turn in response to an object. The other strategy is called **allocentric**. It involves the construction of an internal representation of space in which known objects are accurately mapped in terms of their spatial relationships. Such cognitive maps allow an animal to locate a particular point in space from different starting points and to choose a novel route to a goal point. Cognitive maps also allow an ordered exploration of a new environment, such that the animal remembers the location of each visited part as it explores the new space. It can thus methodically and efficiently explore the entire space without returning to already visited locations. In tests that used a variety of armed mazes, goldfish were found to be able to use both egocentric and allocentric strategies—sometimes both strategies simultaneously—to deal with spatial aspects of their environment. That they could employ allocentric strategies suggested that a hippocampal-like component of their pallium might be present.

Due to the eversion process during embryological development, the distal part of the pallium would correspond topologically to the hippocampal formation of non-

actinopterygian vertebrates, and the more proximal part, Dm, would correspond to the amygdalar formation. In the distal part of the pallium is an area that receives a heavy olfactory input, called the posterior part of the dorsal zone, or Dp. Next to it lies Dlv, which appears to be the best candidate for the hippocampus. In contrast, the proximally situated Dm is the best candidate for the amygdala. Olfactory inputs terminate in the more ventral part of Dm, suggesting that that part may correspond to the olfactory amygdalar components of amniotes. The more dorsal part of Dm receives various ascending sensory pathways, indicating that it may correspond to the amniote frontotemporal amygdala.

Salas, Rodríguez, Broglio, and their other colleagues investigated the neural basis for spatial mapping and other functions of the goldfish telencephalon. Their series of behavioral studies following various lesions to parts of the pallium—either in its dorsolateral part involving Dlv or in its medial part involving Dm—have produced a formidable amount of data in support of hippocampal-like functions of memory and spatial mapping for Dlv and amygdala-like functions, such as involvement in fear conditioning, for Dm. For example, lesions of Dlv but not of Dm result in deficits in spatial tasks but not in visually cued tasks. They also impair spatial exploration in novel environments and impair performance on a variant of the Morris water maze apparatus, which is commonly used for spatial memory studies with rats. The subject swims to a platform that is slightly under the surface of the water and thus invisible to the swimmer. The subject has to remember the location of the platform relative to various visual cues in the room. This maze was ingeniously adapted for goldfish using a series of small-diameter tubes placed in a grid pattern under water, such that the goldfish needs to use similar visual cues in the room

BOX 30-I. The Hippocampus and the Amygdala of Goldfish—cont'd

to return to the particular tube in which a food reward is located. Goldfish with lesions of Dlv have profound deficits in this task, whereas those with lesions of Dm do not.

Not only lesion studies support the comparison of Dlv to the hippocampus in evaginated pallia. During spatial learning and memory tasks, intracellular morphological changes occur that can be localized anatomically. Ribosomal RNA synthesis occurs in the involved neurons, particularly localized in the nucleolar organizer region (NOR) of the cell nucleus. Argyrophilic NOR-associated proteins (AgNOR) can be stained and visualized histologically, and their size, which increases during protein synthesis, can be measured. After goldfish undergo spatial learning, the AgNORs in Dlv are significantly enlarged, while those in the cells of other pallial areas, including Dm, are not. This finding strongly supports the involvement of Dlv in spatial and memory functions.

In contrast to the hippocampal functions of Dlv, Dm is involved in amygdala-like functions. Goldfish can be conditioned to increase their heart and respiration rate in a paradigm that pairs a light stimulus with a subsequent, mild electric shock to a fin. Both the acquisition and retention of this association is impaired following lesions to Dm, but it is left intact in goldfish with lesions to Dlv. Thus, the simple eversion model, with the distal pallial region Dlv corresponding to the position of the hippocampus and the proximally lying Dm corresponding to the amygdala, is supported by these findings.

As discussed in Chapter 1, functional similarity is generally not regarded as a criterion for homology. Such functional correspondences could be the result of convergent evolution. By this logic, Dlv might be analogous to the hippocampus but not homologous to it, and likewise, Dm might be analogous to the amygdala but not homologous to it. On the other hand, most homologous structures have similar functions, so the similarity of function in this case may well be consistent with homology. The type of homology needs to be considered, however. Dlv and Dm may or may not have been present in the common ancestor of actinopterygian fishes, since they have not been identified in cladistian or sturgeon brains. Nonetheless, while possibly not historically homologous by the criteria that this comparison requires, these structures may well be syngenous, i.e., generatively homologous. The basic sets of patterning genes for the medial-to-lateral—or distal-to-proximal—layout of the pallial surface were most likely inherited from a deep common ancestor of the vertebrate radiation. This would imply that there are medially/distally expressed pat-

ternern genes for pallial tissue that is able to carry out spatial mapping and memory functions and likewise laterally/proximally expressed patterning genes that specify pallial tissue for emotional learning, such as being able to acquire fear conditioning.

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THE LIMBIC PALLIUM IN AMNIOTES (GROUP IIB)

Nuclei form the pallial parts of the telencephalon in Group IIA vertebrates; however, both nuclei and cortices

are present in the pallium in Group IIB vertebrates. In this section, we will first compare the pallial parts of the limbic system among mammals, reptiles, and birds. We will then consider the subpallial limbic structures in these three groups of amniotes, as well as across the major amniote taxa.

BOX 30-2. Imaginative Images of the Hippocampus

Before discussing the hippocampal formation and limbic system of mammals, we will pause briefly to consider some aspects of their rather creative nomenclature. The term hippocampal formation is used here to designate the **hippocampus proper** (Ammon's horn), the **dentate gyrus**, and their related transitional cortices, that is, the **subicular** and **entorhinal cortices**. The term **limbic lobe** was introduced by the French neuroscientist Pierre Paul Broca in 1878 to refer to the hippocampal formation and the cingulate gyrus, parahippocampal gyrus, and related cortices, which medially border the surrounding neocortical cortices. The French noun *limbe* means border or halo, and the adjective *limbique* thus means bordering. The term **limbic system** was introduced by the American neuroscientist Paul MacLean in 1952 to encompass the limbic lobe and related subcortical structures, including the amygdala (meaning "almond"), septal nuclei (septum meaning "wall"), and related parts of the striatum and diencephalon.

The term hippocampus is of much earlier origin than the "limbic" terminology. In an extensively researched paper published in 1923, Frederic Lewis discussed the origin of the terms hippocampus and Ammon's horn and their use in neuroanatomy. The term hippocampus was introduced in the sixteenth century by Julius Caesar Arantius, a student of Andreas Vesalius. The same name is used for the teleost fish with the common name of seahorse. Lewis stated that "The flight of fancy which lead Arantius, in 1587, to introduce the term *hippocampus* is recorded in what is perhaps the worst anatomical description extant. It has left readers in doubt whether the elevations of cerebral substance were being compared with fish or beast, and no one could be sure which end was the head." Part of the difficulty seems to stem from Arantius's use of two different names for this structure: hippocampus and *vermis bombycinus*, or silkworm (Fig. 1).

The derivation of the word hippocampus most frequently given is from the Greek *hippos* for "horse" and *kampos* "sea monster." Lewis preferred a derivation based on *hippos* (horse) and *kampia* (caterpillar)—a horse-headed caterpillar. The latter seems consistent with the silkworm of Arantius's alternative name. In any event, Lewis concluded with the wistful opinion "How Arantius pictured his sea-horse may remain forever recondite. . . ."

The hippocampus is also called Ammon's horn, or *Cornu Ammonis*, to use its Latin name, for its equally poorly perceived likeness to a ram's horn. The term ram's horn was introduced by the Danish anatomist, Jakob Benignus Winslow in 1732 before being superseded in 1742 by the more elaborate term Ammon's horn, first used by the French anatomist René Jacques Croissant de Garengéot. The term Ammon's horn was derived from the name of an Egyptian god, Amun Kneph, a god the Egyptians depicted either as a ram or as a human with ram's horns.

Some of the constituents of the hippocampus also have imaginative names: the *alveus*, which is a "trough" or a

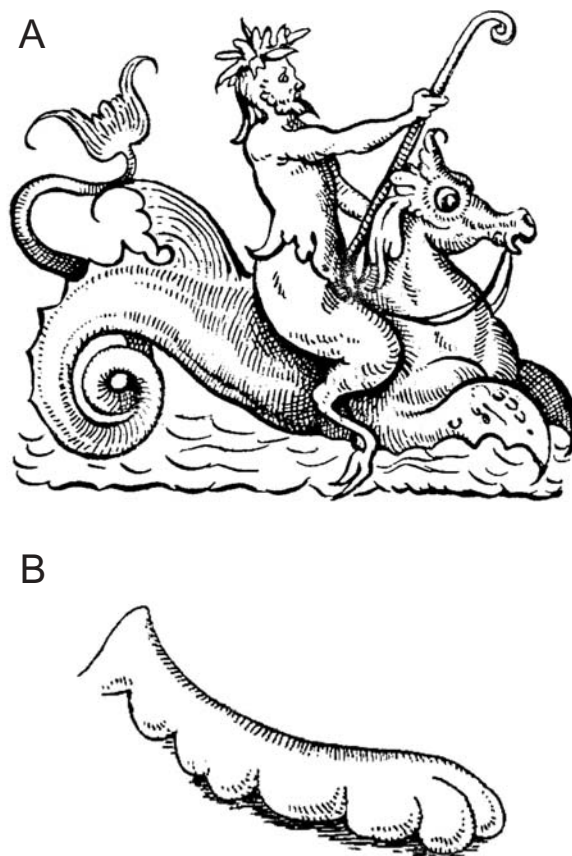


FIGURE 1. Two artistic conceptions of the hippocampus. A: the hippocampus of Greek mythology with the head of a horse and the body of a fish. B: the *vermis bombycinus* (silkworm) of Arantius. Adapted from Lewis (1923) and used with permission of John Wiley & Sons.

"hollow," the *fimbria*, which is a "fringe," and the *subiculum*, which is a "support" or an "underlying structure." Finally, the *fornix*, which is Latin for "arch," has a clearly arched appearance, and thus agreement seems to be universal that this is an appropriate name.

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Limbic Pallium of Mammals

The hippocampal formation of monotremes and marsupial mammals is similar topologically to that in nonmammalian amniotes in that it lies along the medial wall of the hemisphere (Fig. 30-9). In adult placental mammals, the hippocampal formation also occupies the medial wall of the hemisphere, but its relationships with other structures are distorted by the greatly expanded neocortical areas. In some placental mammals, such as rodents and sheep, the hippocampus has a dorsal and ventral part, with the dorsal part maintaining its topologically medial position as in marsupials. In others, such as primates, the more dorsal part is reduced to a very thin strip of tissue called the **induseum griseum**, and the hippocampal formation is otherwise limited to the more ventral position, tucked into the temporal lobe. The hippocampus also folds inwardly during development so that the dentate gyrus, a prominent layer of closely packed neuron cell bodies, is innermost. Although not obvious in transverse sections, in sagittal sections the cellular layer of the dentate gyrus appears as a series of waves or notches, like a row of teeth, and the gyrus is named for this attribute.

A horizontal section through part of the hippocampal formation in a rodent is shown in Figure 30-10. The dentate gyrus caps the end of the curved hippocampus, or Ammon's horn (see Box 30-2). The hippocampus is divided into four "fields" on cytoarchitectural grounds, and the fields are referred to as **CA1–CA4**, "CA" being the abbreviation for Ammon's horn: *Cornu Ammonis*. The cortical region adjoining the CA1 field of the hippocampus is called the subicular region and has three subdivisions that are, in medial-to-lateral order, the **subiculum**, the **presubiculum**, and the **parasubiculum**. Entorhinal cortex adjoins the parasubiculum.

The location of the initial part of the largest efferent pathway from the hippocampal formation, the **fornix**, is also shown in Figure 30-10. Its main components are the axons of hippocampal (CA) and subicular neurons that project to multiple sites, including nuclei within the septum and hypothalamus. Because the axons accumulate on the surface of the CA region, they are referred to as the **alveus**. For a short distance where they coalesce into a discrete, extrahippocampal bundle, they are called the **fimbria**, and from there on, they are called the fornix, which arches in the sagittal plane over the region of the diencephalon.

Figure 30-11 illustrates the hippocampal formation of primates. During embryological development, the hippocampal formation rotates inward, as noted above [Fig. 30-11(B)]. For orientation, an enlargement of the hippocampal region on the right side in the adult human brain is shown in the transverse plane in Figure 30-11(C). The very similar hippocampal formation of a rhesus monkey is shown at the lower right of this figure (in panels D and E), with a drawing and Nissl photomicrograph.

In the dentate gyrus, the majority of neurons have spherical- to oval-shaped cell bodies and are called **granule cells**. Modified pyramidal cells are also present, as are other neurons called basket cells. Ammon's horn is composed primarily of large and small pyramidal cells, some of which are **double pyramidal cells**, since their dendritic arborizations extend in two polar directions away from the cell body. Smaller interneurons are also present. The large pyramidal cells contribute to the fornix. The major gateway for inputs relayed into the hippocampus is the entorhinal cortex (Fig. 30-12). Entorhinal cortex receives an array of inputs from parts of the ventral portion of the temporal lobe, part of the frontal lobe called the orbitofrontal cortex, cortices neighboring the entorhinal

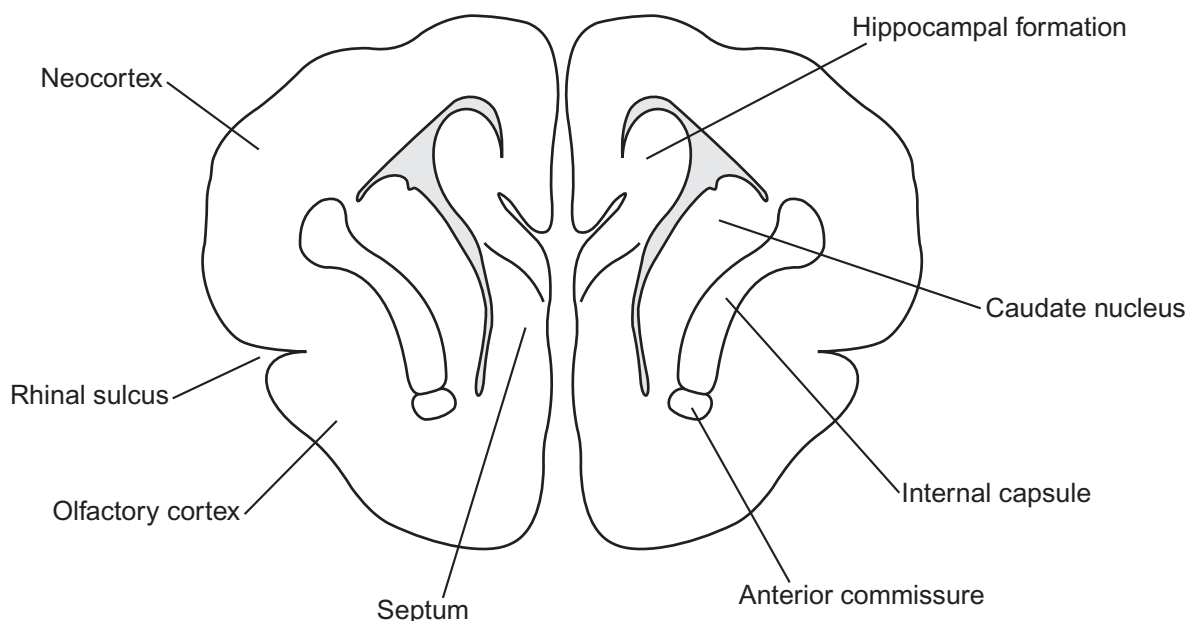


FIGURE 30-9. Drawing of a transverse section through the telencephalon of a marsupial (*Hypsiprymnus rufescens*). The ventricular spaces are indicated by light gray shading. Data from Ariens Kappers et al. (1967).

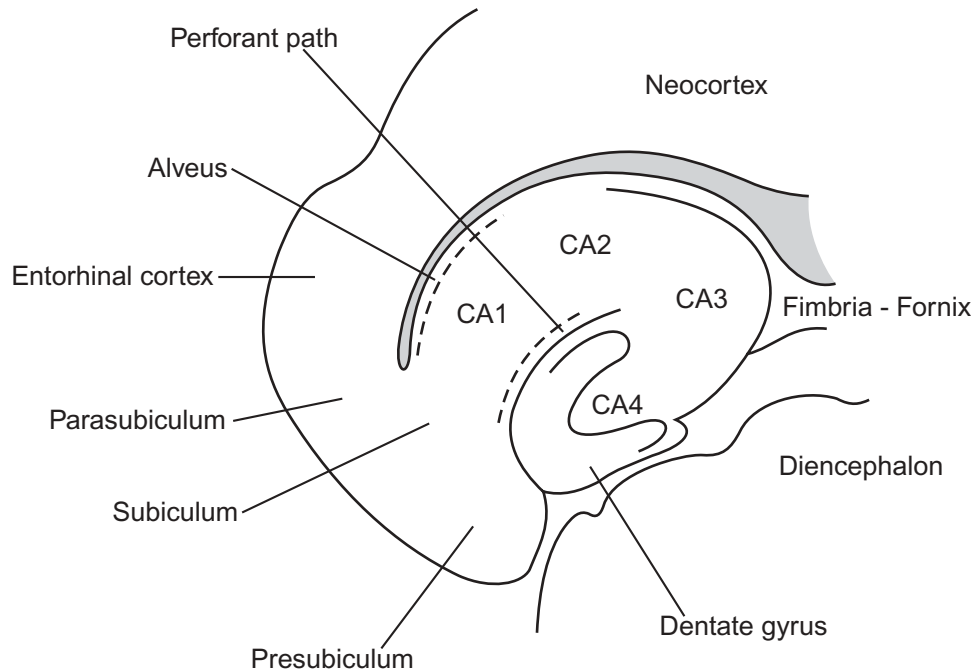


FIGURE 30-10. Drawing of a horizontal section through the left hippocampal formation of a rat. Fields CA1–CA4 constitute the hippocampus proper. The part of the lateral ventricle present in this region is indicated by shading. Adapted from Isaacson (1982) and used with kind permission of Springer Science and Business Media.

cortex, primary sensory cortices, the septal nuclei, and numerous subcortical structures. Many of the cortical connections of entorhinal cortex are reciprocal ones, and these are shown in the figure. Entorhinal cortex also receives a major input from the cingulate gyrus, which will be discussed further below.

Entorhinal cortex projects to some of the CA fields of the hippocampus and to the dentate gyrus, which also projects to the hippocampus. Part of this projection arises from the more medial, or proximal, part of the entorhinal cortex, nearer to the subiculum. It is to the more superficial part of the hippocampal formation and is thus called the **alvear pathway**; it terminates on the outer dendritic arbors of the hippocampal and dentate gyrus cells. A second projection arises from the more lateral, or distal, part of the entorhinal cortex, and that pathway runs in a more interior position, deep to the layer of hippocampal pyramidal neurons. It is known as the **perforant pathway**.

Although the actual situation for the entorhinal-hippocampal projections is more complex and overlapping, a so-called **trisynaptic loop** has been identified and is indicated by the thick gray arrows in Figure 30-12. The name of this loop is somewhat misleading, because it schematically involves a minimum of five synapses rather than three, and of course in reality, it involves thousands of neurons. The basic loop consists of the set of projections from entorhinal cortex to the dentate gyrus, the dentate gyrus to CA3, CA3 to CA1, CA1 to the subiculum, and the subiculum back to entorhinal cortex. Within the trisynaptic loop, the axons of the dentate gyrus neurons are rich in zinc and are called **mossy fibers**. The CA3 to CA1 projection is accomplished by numerous collateral pro-

jections from CA3 axons to the CA1 region as the former run into the alveus to form the fornix. These collateral branches are called **Schaffer collaterals**.

As indicated in the figure, the trisynaptic loop is augmented and even overshadowed by additional components that include 1) a direct projection from the dentate gyrus to CA1, 2) direct and reciprocal connections between entorhinal cortex and CA1, and 3) direct and reciprocal connections between CA1 and the frontotemporal amygdala. Additionally, the frontotemporal amygdala projects reciprocally to the entorhinal cortex, which in turn projects reciprocally to the subiculum. All of these pathways combine to produce a feed-forward, excitatory circuit through the hippocampal formation that then interacts with the subiculum, entorhinal cortex, and frontotemporal amygdala.

Both the subiculum and the entorhinal cortex have substantial reciprocal projections with widespread areas of association cortices. The frontotemporal division of the amygdala likewise has extensive, reciprocal cortical connections. The trisynaptic loop is thought to be crucial for the maintenance of short-term memory, whereas the reciprocal cortical connections achieved through the entorhinal and subicular cortices and through the frontotemporal amygdala allow for long-term storage of memories. The subicular cortices also project to nucleus accumbens and the olfactory tubercle, that is, the ventral striatum, which is the site of an important interface between the limbic and striatal systems (see Chapter 24).

The second major set of afferent connections to the hippocampal formation involves the fornix system, which also carries efferent fibers. The fornix interconnects the hip-

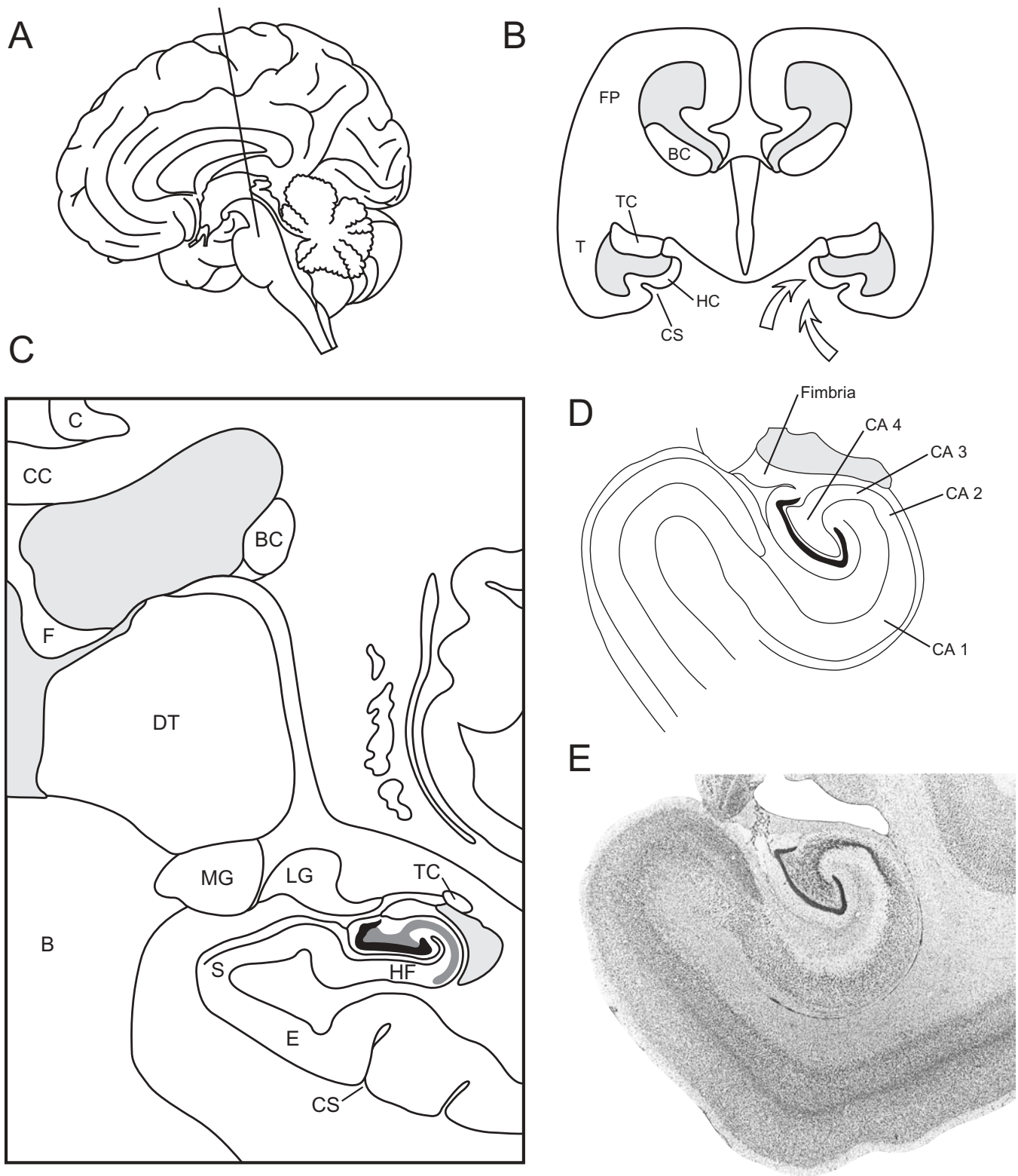


FIGURE 30-11. The hippocampal formation in primates—human (*Homo sapiens*) in A–C and macaque monkey (*Macaca mulatta*) in D and E. A: sagittal section with line indicating the level and angle of the transverse hemisection through the right hippocampal formation of the human brain shown in C. The internal rotation of the hippocampal formation within the temporal lobe during development is indicated by the arrows on the right side in the transverse section in B. Enlarged drawing (D) and Nissl photomicrograph (E) of a transverse section through the right hippocampal formation of the macaque monkey are also presented. In B, C, and D, ventricular areas are indicated by light shading. Abbreviations: B, brain-stem; BC, body of caudate nucleus; C, cingulate gyrus; CA1–CA4, *Cornu Ammonis* hippocampal fields; CC, corpus callosum; CS, collateral sulcus; DT, dorsal thalamus; E, entorhinal cortex; F, fornix; FP, frontal-parietal neocortex; HF, hippocampal formation; LG, dorsal lateral geniculate nucleus; MG, medial geniculate body; S, subicular cortices; T, temporal neocortex; TC, tail of caudate nucleus. C adapted from DeArmond et al. (1989) and used with permission of Oxford University Press. E from Suzuki and Amaral (2003) and used with permission of John Wiley & Sons.

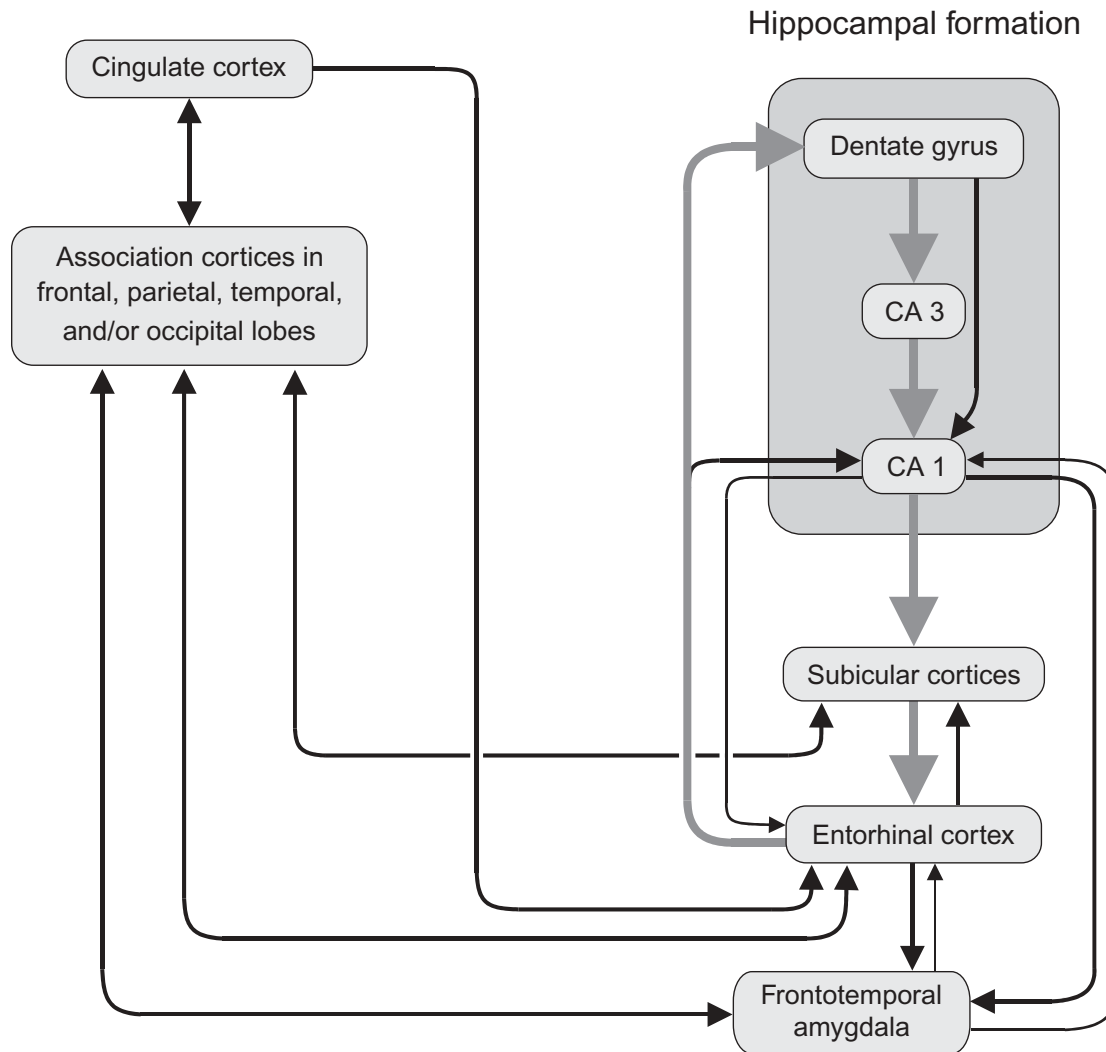


FIGURE 30-12. Diagram of some of the connections of the hippocampal formation in mammals. The thick gray arrows indicate the so-called trisynaptic loop. The black arrows indicate other connections, and the thickness of these arrows indicates the relative strength of the projection. Partly based on Von Bohlen und Halbach and Albrecht (2002).

hippocampal formation with nuclei in the septal area, diencephalon, and more caudal brainstem. A circuit within this system (Fig. 30-13), recognized by and named for the American neuroscientist James Papez, involves projections from the mammillary body in the hypothalamus to the anterior nuclear group of the dorsal thalamus and thence to the cingulate gyrus. The cingulate gyrus then projects to entorhinal cortex, which in turn projects to the subicular cortices and Ammon's horn, as well as to the dentate gyrus. Ammon's horn and the subicular cortices project back, via the fornix, to the mammillary body. Papez proposed that this circuit might be involved in functions related to both the experience and expression of emotions. Numerous additional interconnections have subsequently been identified within this circuit, including direct projections from the mammillary body and supramammillary nucleus to the hippocampal formation (not shown in Fig. 30-13), from the anterior nuclear group of the dorsal thalamus to

the subiculum, and from the subiculum and Ammon's horn to the anterior nuclear group. In identifying this circuit, Papez recognized the fundamental role of the limbic system as an interface between emotions and cognitive processes.

The hippocampal formation receives additional afferent connections, primarily via the fornix. Dorsal thalamic nuclei of the medial nuclear group, particularly nucleus reuniens, and the paraventricular nuclei of the epithalamus also project to the hippocampal formation. As discussed in Chapter 21, the paraventricular nuclei have reciprocal connections with the amygdala and with lateral hypothalamic and preoptic areas as well as with the hippocampal formation. Similarly, the medial habenula is involved in a limbic circuit, discussed below in conjunction with the septal nuclei. Monoaminergic projections from the locus coeruleus and serotonergic inputs from the midbrain raphe also reach the hippocampal formation.

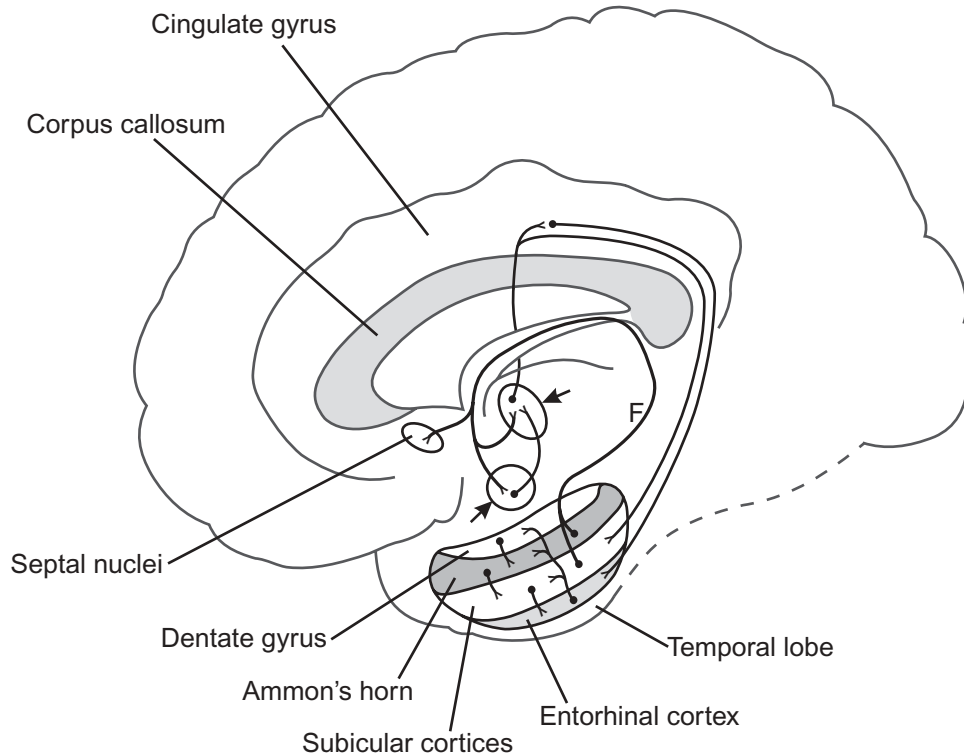


FIGURE 30-13. Semischematic drawing of a parasagittal section showing some of the connections of the hippocampal formation, particularly Papez's circuit. Rostral is toward the left. The size of the hippocampal formation has been exaggerated to show detail. Nucleus anterior of the dorsal thalamus is indicated by the upper arrow and the mammillary body of the hypothalamus by the lower arrow. F indicates the fornix.

An important input to the limbic telencephalon arises from the dopamine-containing cells of the ventral tegmental area (VTA) in the midbrain. This system has been referred to as the mesolimbic dopamine system, in contrast to the dopaminergic projections from the substantia nigra (SN) to the striatum. Recent findings show that significant overlap exists in the projections of both the substantia nigra and the ventral tegmental area to both the limbic system and the striatum, and thus the two sets of projections alternatively can be considered as a unitary, **mesotelencephalic dopamine system**. Various combinations of neurons in the VTA or the SN or both also project to limbic cortices including the cingulate cortex, entorhinal cortex, and the hippocampal formation. They additionally project to related parts of neocortex, including the prefrontal cortex, as well as to subpallial limbic structures as discussed below. This ascending dopamine system has been implicated in a wide range of functions, including reward aspects of learning and various cognitive functions. In humans, abnormally high levels of dopamine are correlated with symptoms of schizophrenia.

Damage to the hippocampal formation in mammals results in a number of changes in behavior, including increased locomotor activity, decreased distractibility, and severe impairments of learning and memory. Hippocampal memory deficits prevent the accumulation of new knowledge, although memory of events that occurred prior to the damage is preserved.

Limbic Pallium in Nonmammalian Amniotes

Reptiles. In reptiles (Figs. 30-14–30-16), the medial pallium is a cortical lamina of cells that is divided into two parts: **medial cortex (MC)** and **dorsomedial cortex (DMC)**. These two parts of the medial pallium are also referred to as the **small-celled** and **large-celled parts**, respectively. A **dorsal cortex (DC)** is also present and divisible into two parts. The dorsal cortex traditionally has been recognized as the homologue of at least part of the nonlimbic neocortex of mammals, but some of its features need to be considered here along with those of the medial pallium in regard to the limbic system of amniotes. The lateral part of the dorsal cortex receives visual input relayed from the retina by the dorsal lateral geniculate nucleus and has been discussed in Chapter 26. Some of the connections of the medial part of the dorsal cortex resemble limbic system connections of mammals and will be included here.

In reptiles, the medial pallium is a three-layered cortex. The majority of neuron cell bodies lie in the middle layer, **layer 2** (Fig. 30-14), and most of their dendrites branch in the most superficial layer, **layer 1**. A few neuron cell bodies are present in both layer 1 and the deepest layer, **layer 3**. In some snakes (Fig. 30-15), an additional layer of densely packed cell bodies is present ventral to the dorsomedial cortex and is called the **ventral cell plate**.

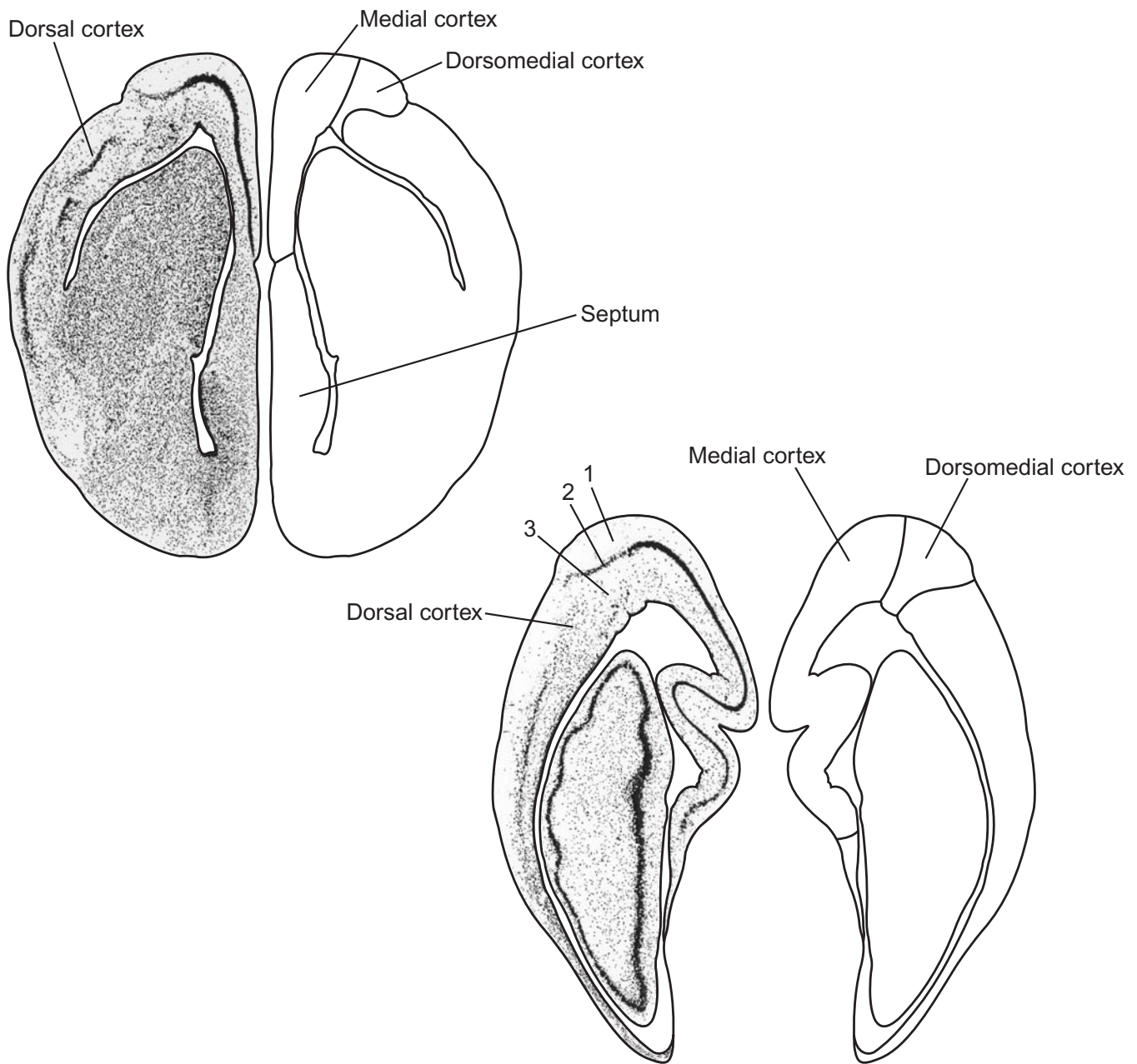


FIGURE 30-14. Transverse hemisections with mirror-image drawings through the telencephalon of a lizard (*Tupinambis nigropunctatus*). The top section is more rostral. The numbers 1, 2, and 3 indicate layers of cortex. Adapted from Ebesson and Voneida (1969) and used with permission of S Karger AG, Basel.

The majority of cells in layer 2 of the medial cortex are densely packed and characterized as small **double pyramidal cells**, or **bitufted cells** [Fig. 30-17(C-E)], similar to the double pyramidal cells of mammals and named in reference to the fact that dendrites of these cells extend in both superficial and deep (diametrically opposite) directions. Multiple types of bitufted, Golgi type I cells are present, as are Golgi Type II local circuit interneurons, such as that shown in Figure 30-17(B). Layer 1 of medial cortex contains few cells, most of which are either stel-

late or horizontal. A moderate number of cells are present in layer 3 and are of variable morphology, including spiny multipolar, pyramidal, and horizontal types.

Neurons in the dorsomedial cortex are primarily concentrated in layer 2 and consist of double pyramidal cells that are larger than those in the medial cortex. Their apical dendrites also ramify extensively in layer 1, and their basal dendrites ramify in the superficial part of layer 3. The axons of these cells enter the alveus in the deep part of layer 3. Bipolar cells are

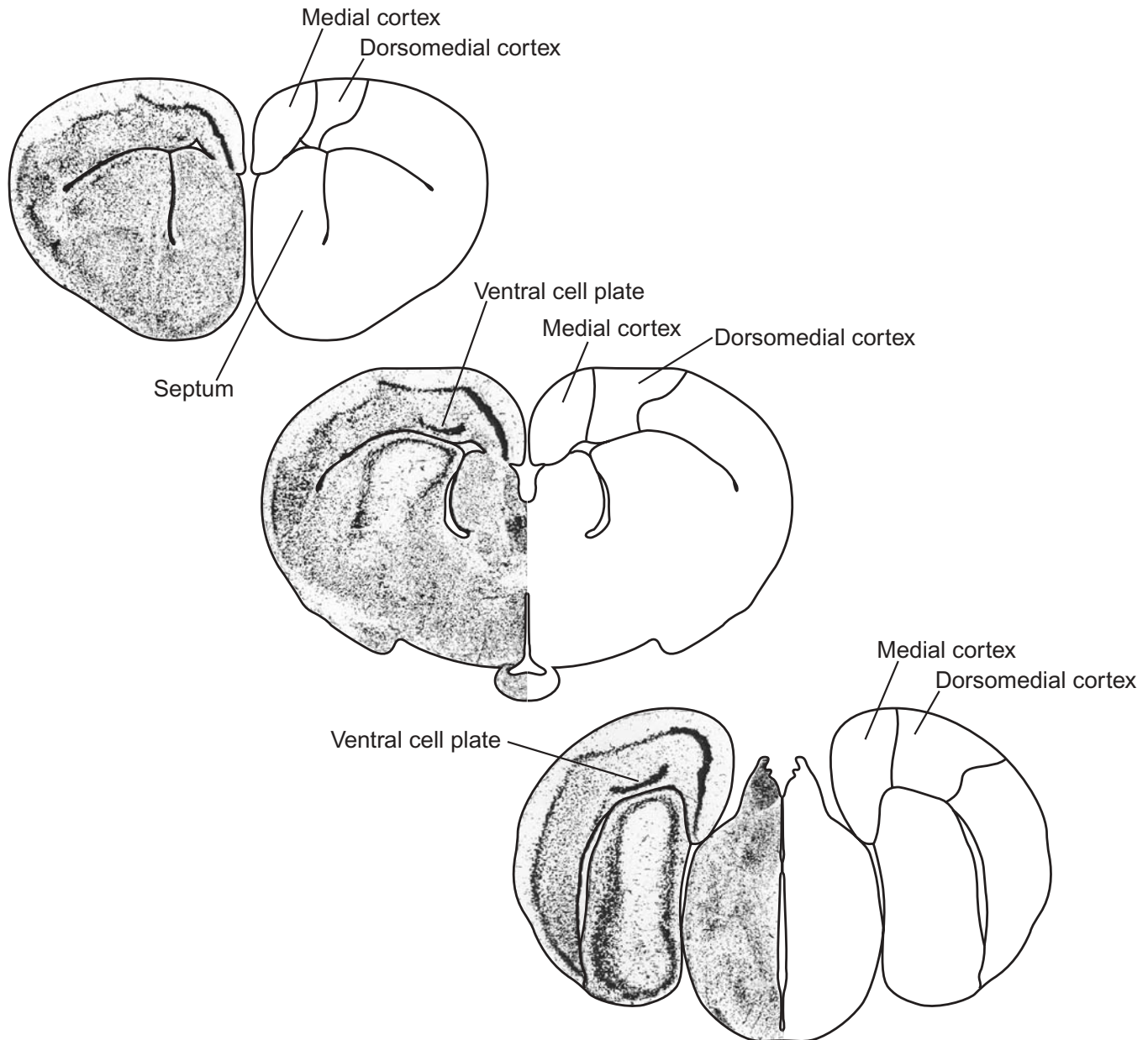


FIGURE 30-15. Transverse hemisections with mirror-image drawings through the telencephalon of a snake (*Eryx johni*). The most rostral section is at the top. Adapted from Ulinski (1974) and used with permission of John Wiley & Sons.

present in layer 1 of the dorsomedial cortex, and several cell types, including double pyramidal, multipolar, and horizontal, are present in layer 3.

Figure 30-17 contrasts some of the various types of bitufted cells found in lizards with a typical neuron of the medial pallium in a frog, shown in part A of the figure. This neuron in the frog lacks a basilar dendritic ramification but is nevertheless a Golgi Type I projection neuron, giving rise to an axon that projects to a number of different extrinsic sites. It would appear that bitufted neurons, or double pyramidal cells, are an apomorphic feature of amniotes.

The medial cortex in reptiles receives afferent projections from several other cortices in the telencephalon, while the

dorsomedial cortex is primarily interconnected with just the medial cortex. The lateral (olfactory) cortex, the dorsal cortex, and the dorsomedial cortex project to the medial cortex. The medial cortex projects back reciprocally to the dorsal and dorsomedial cortices and is also reciprocally connected with the septum. The dorsomedial cortex has a substantial commissural connection with the contralateral dorsomedial cortex, in addition to its reciprocal connection with the medial cortex, and receives an input from the septum. Ascending inputs to the medial and dorsomedial cortices are similar and include projections from the anterior dorsolateral nucleus of the dorsal thalamus, the mammillary and periventricular parts of the

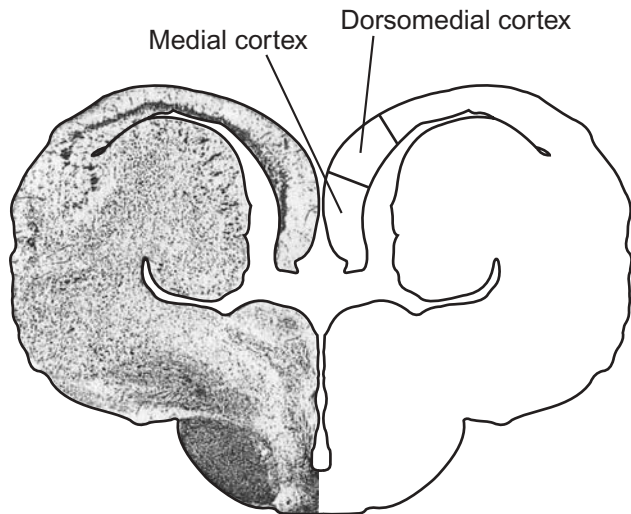


FIGURE 30-16. Transverse hemisection with mirror-image drawing through the telencephalon of a turtle. Adapted from Balaban and Ulinski (1981) and used with permission of John Wiley & Sons.

hypothalamus, the raphe nuclei, the locus coeruleus, and the reticular formation.

Connections of the medial part of the dorsal cortex that resemble those of the limbic system of other vertebrates include efferent projections to the septal nuclei, amygdalar nuclei, nucleus accumbens, striatum, and hypothalamus. Like the medial and dorsomedial cortices, the dorsal cortex also receives afferent projections from the anterior dorsolateral nucleus of the dorsal thalamus, the mammillary nuclei of the hypothalamus, the raphe, and the locus coeruleus, and, as discussed above, is reciprocally connected with the medial cortex.

Based on similarities in cytological characteristics of the neurons, some of the afferent connections, and the laminar arrangement of the sets of terminal fields in layer 1 from various afferent sources, the medial cortex has been compared with the dentate gyrus in the hippocampal formation of mammals. Likewise, the dorsomedial cortex has been compared with Ammon's horn. These comparisons are supported by recent immunohistochemical findings on the presence of similar subpopulations of GABA neurons in the dorsomedial cortex of lizards and in Ammon's horn in mammals. The medial part of the dorsal cortex has been compared with parts of the mammalian limbic system that border Ammon's horn, that is, the subiculum, the entorhinal cortex, and/or adjacent cortices that lie in a transitional position between the hippocampal formation and neocortex. The topological order of these cortices in reptiles on one hand and in mammals on the other may thus be the same: the sequence of medial cortex to dorsomedial cortex to the medial part of dorsal cortex corresponding to the sequence of dentate gyrus to Ammon's horn to subicular and entorhinal cortices.

Birds. In the telencephalon of birds, the medial pallium contains two laminae of densely packed neurons, which in its ventral part form a "V" shape (Fig. 30-18) and are collectively

referred to as the **hippocampus**, and a region of more diffusely scattered neurons called the **parahippocampal area**. Five different regions within the hippocampal formation (HF) have been recognized in zebra finches and also in pigeons. In the latter, the "V" of cells is divided into lateral (VL) and medial (Vm) parts, and the previously labeled parahippocampal region is divided into three regions, a dorsolateral hippocampal formation (DL), and a dorsomedial HF with a dorsal (DMd) and ventral (DMv) divisions.

The hippocampus and parahippocampal area of birds are homologous, at least as a field, to the medial pallium of reptiles and mammals. Whether the topological arrangement of its components is the same, however, has been a matter of debate (Fig. 30-18). Instead of a topology going from medial (ventral) to lateral, in the order of dentate gyrus to Ammon's horn to subicular and entorhinal cortices as is present in mammals, the topological order in birds has been argued to be Ammon's horn most ventrally (VL and Vm) to dentate gyrus and/or subicular cortex and perhaps then entorhinal cortex most dorsolaterally. The latter regions together comprise DL, DMd, and DMv. Support for this interpretation has come from both immunohistochemical markers and recent studies of intrahippocampal connections. Multiple immunohistochemical markers—including those for acetylcholine, catecholamine, GABA, serotonin, and a variety of neuropeptides—have indicated that the hippocampus of birds, the V-shaped formation of neuron cell bodies, is homologous to Ammon's horn of mammals and that the parahippocampal area of birds is homologous to the dentate gyrus.

The internal circuitry of the hippocampal formation also has been interpreted in favor of the V-shaped formation most closely resembling Ammon's horn. Extrinsic inputs are relayed into DL and DMd, which in turn project to both parts of the V-shaped formation, VL and Vm. Additionally, Vm projects to VL. This pathway has been compared to the projection from entorhinal cortex (the extrinsic source) to the dentate gyrus—which would be DL and DMd—and from there to both CA1 and CA3, with CA3 also projecting to CA1. In the pigeon, Vm thus has been argued to resemble CA3, with VL resembling CA1. Vm and VL in turn project to DMv, which would thus resemble the subiculum of mammals. This feed-forward loop in birds would thus correspond to the so-called trisynaptic loop of mammals.

As is apparent from this comparison, the similarity of the V-shaped formation to Ammon's horn is rather strongly supported, while the particular cell groups that might be dentate gyrus, subiculum, and/or entorhinal are less clearly apparent. These cell populations may be present in the dorsomedial and dorsolateral portions of the formation but not as separately delimited as in mammals. Extrinsic projections arise mostly from the dorsolateral part of the formation, however, supporting the interpretation of it as subiculum. The extrinsic projections are generally similar to those in mammals and reptiles and include those to the septal region, several dorsal thalamic nuclei, and the mammillary region of the hypothalamus.

Despite the points just discussed, the situation is far from being resolved. Recently, Yasuro Atoji and Martin Wild proposed a different view of the circuitry and hippocampal components in birds. Based on their findings on the intrinsic connectivity of this region, they proposed that the V-shaped formation is,

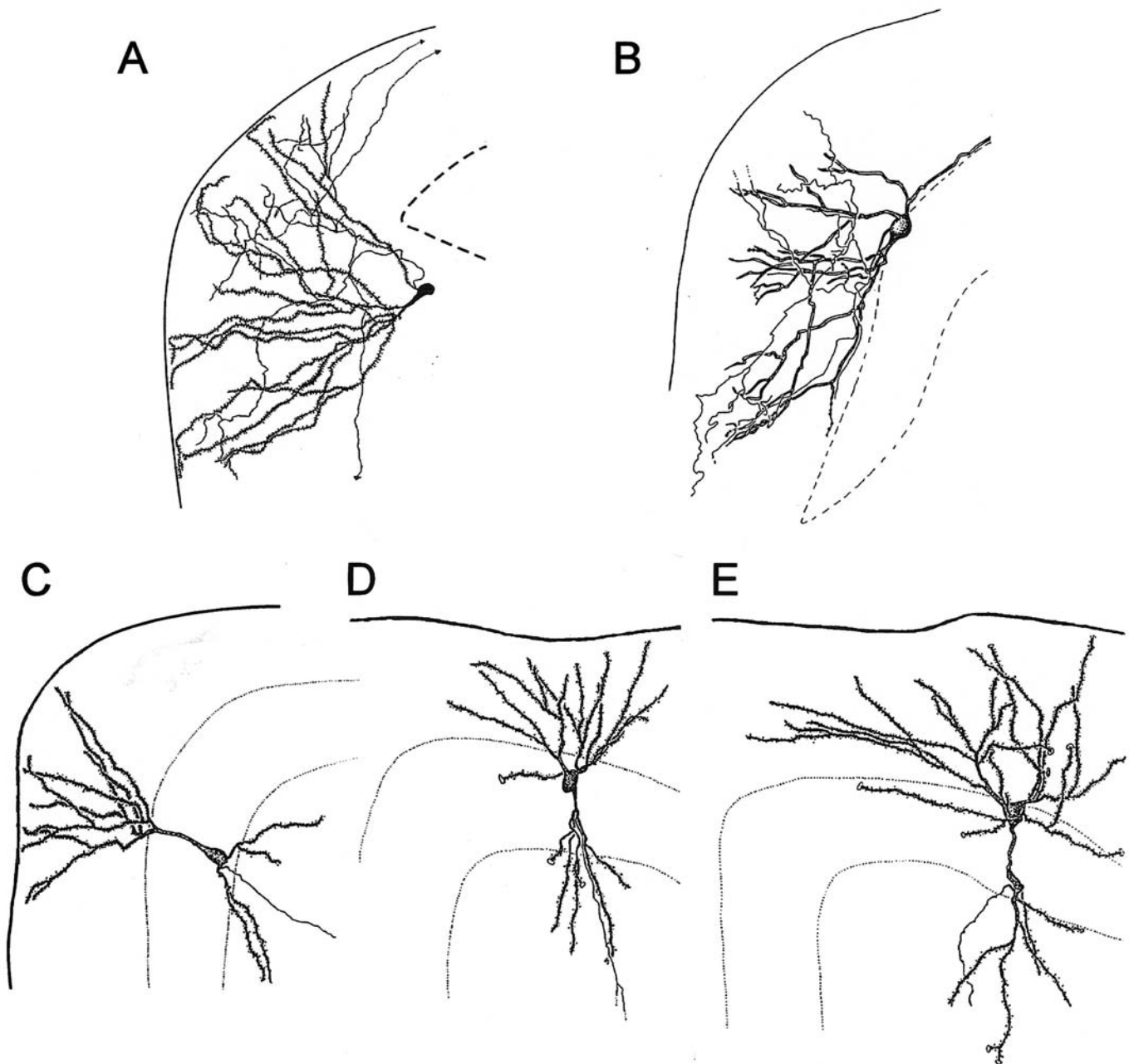


FIGURE 30-17. Neurons of the medial pallium in a salamander (*Plethodon jordani*) (A) and a lizard (*Podarcis hispanica*) (B–E). The neuron shown in A is an extrinsically projecting neuron, as are those in C–E. The neuron in B, in contrast, is an intrinsic neuron. Cells with bipolar dendritic trees, such as those in C–E, are absent in amphibians. A adapted from Westhoff and Roth (2002), B from Luis de la Iglesia et al. (1994), and C–E from Luis de la Iglesia and Lopez-García (1997). All parts of this figure used with permission of John Wiley & Sons.

after all, homologous to the dentate gyrus of mammals and that DM comprises components of both Ammon's horn and the subiculum. If this is the case, the topology of the system would be the same as in mammals and lizards, and no alteration of it would have occurred within the diapsid line. This would in fact be the more parsimonious explanation. Additional research on the medial pallium of birds will be needed to provide a definitive resolution to this issue; because crocodiles, among rep-

tiles, are most closely related to birds, studies of their medial pallial connections would be of value as well.

Despite potential topological differences, as in other vertebrates, the hippocampal formation in birds is highly involved in spatial mapping. For example, the hippocampal formation is essential for the ability of homing pigeons to use spatial landmarks in navigation, as Verner Bingman and his co-workers have shown. That these and other birds use environmental land-

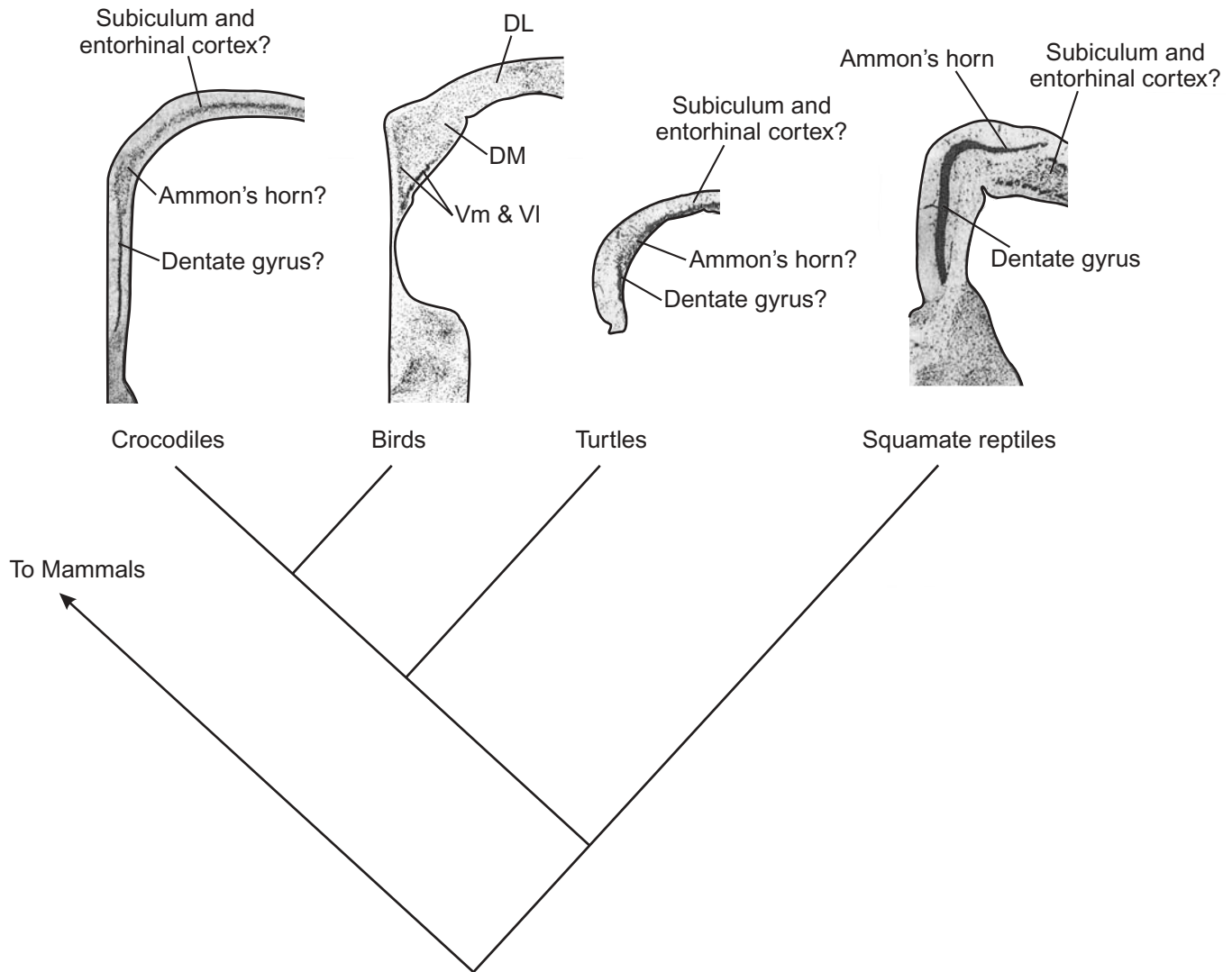


FIGURE 30-18. Comparison of medial pallial organization in extant nonmammalian amniote groups. For each medial pallium shown, dorsal is toward the top and medial toward the left. Abbreviations used for bird medial pallium: DL, dorsolateral hippocampal formation; DM, dorsomedial hippocampal formation; VI & Vm, lateral and medial parts of V-shaped formation.

marks in finding their way to their goal location is well established, and just as in mammals, the hippocampus plays a key role in this process.

The degree of development of the avian hippocampal region has also been found to be related to the spatial memory of the location of stored food, as Sara Shettleworth and other investigators have established. Birds that store and then retrieve food have significantly larger hippocampal formations than related species that do not store food. This hippocampal enlargement has occurred independently at least three times in different groups of birds: titmice, corvids, and nuthatches.

LIMBIC SUBPALLIUM: SEPTUM

Although the septal area includes a small pallial component, most of this region lies within the subpallium, situated in

the medial wall of the telencephalon. Septal nuclei have been identified in a variety of anamniotes, but only limited information is available on their connections or histochemistry. In lampreys, a septal nucleus has been identified; it receives an input from the olfactory bulb, and it projects to the medial pallium. In squalomorph sharks (Fig. 30-2), a septal nucleus lies in the ventromedial part of the telencephalon. In nonteleost ray-finned fishes (Fig. 30-3), the **ventral nucleus of the ventral telencephalic area (Vv)** is a strong candidate for a homologue of the septal region of other vertebrates, and it also may include a nucleus accumbens-like component. In lungfishes (Fig. 30-4), a septal area, called the **medial subpallium**, lies ventral to the medial pallium. In amphibians (Fig. 30-5), **medial** and **lateral septal nuclei** lie ventral to the medial pallium, and the nucleus of the diagonal band of Broca lies ventral to the septal region.

In hagfishes, a medioventrally lying **septal area** has been tentatively identified. In galeomorph sharks, skates, and rays

(Fig. 30-7), **medial** and **lateral septal nuclei** lie ventral to the medial pallium. In teleost fishes, the ventral parts of the telencephalon (Fig. 30-8) are somewhat less difficult to identify than the various pallial areas, due to topological, connectional, and histochemical data that are less in conflict with the corresponding data for this part of the telencephalon in other vertebrates. As for non-teleost ray-finned fishes, the medially lying **ventral nucleus of area ventralis (Vv)** is considered to be homologous to the septal nuclei of other vertebrates. As discussed in Chapter 24, Vv may be homologous as a field to part of the septum as well as to nucleus accumbens and the substantia innominata. Other nuclei present in this region, including nucleus taenia (NT) and the central (Vc), intermediate (Vi), postcommissural (Vp), and supracommissural (Vs) nuclei, all receive olfactory input and may be components of the olfactory amygdala (as discussed in Chapter 29).

Two main divisions of the septal region are generally recognized in mammals. The lateral division of the septum contains a pair of **lateral septal nuclei**. The medial division of the septum contains the **medial septal nucleus**. The **nucleus of the diagonal band of Broca** is sometimes included within the medial division of the septum, as is done here, and is sometimes referred to as a separate entity. Both the medial septal nucleus and the nucleus of the diagonal band of Broca (both its vertical and horizontal limbs) contain numerous cholinergic neurons. An additional posterior division of the septum is also present and contains the **septohippocampal** and **triangular nuclei**.

The major connections of the septum are reciprocal connections with telencephalic and diencephalic limbic structures and a pathway that forms part of a limbic circuit through the habenula. The septal nuclei receive inputs from the amygdala and from the locus coeruleus. They are reciprocally connected with the hippocampus and the subicular cortices, with the preoptic area and a variety of nuclei in the hypothalamus, including the mammillary complex, and with the dopamine-containing neurons of the ventral tegmental area. The projection from the septal region to the hippocampus arises from the cholinergic neurons of the medial septal nucleus and also from those within the vertical limb of the nucleus of the diagonal band of Broca. Additional septal efferents are to the dentate gyrus and entorhinal cortex, the habenula, and the dorsal raphe nucleus.

The limbic circuit that encompasses the septum and the habenula (see Chapter 21) involves projections from the hippocampus and subiculum to septal nuclei. The medial septal nucleus and the nucleus of the diagonal band project to the medial habenular nucleus, which likewise contains cholinergic neurons and in turn projects to the interpeduncular nucleus. There is also a direct septointerpeduncular nuclear projection. The interpeduncular nucleus projects back to the hippocampal formation.

Although damage to the septal area results in a number of behavioral changes, the results of septal lesions vary significantly among different species, and thus generalizations are somewhat hazardous. In some mammals, including humans, increased rage reactions and hyperemotionality occur immediately following septal lesions, although these behaviors return to normal over time. Animals with septal lesions show hyperresponsiveness to stimuli and also increased aggressive

responses, which may in fact be a manifestation of an increase in defensiveness. Such animals also increase water intake and decrease open-field locomotion.

The septal area in reptiles (Figs. 30-14 and 30-15) and birds is generally similar to that in mammals, indicating conservative evolution of this region, although some interesting differences exist. Most of the connections of the septal nuclei are like those in mammals. In lizards, three main septal area divisions—central, ventromedial, and midline—that together comprise a total of nine septal nuclei, recently have been recognized. As in mammals, the main afferent projections to the septal area arise from limbic structures, including the medial, dorsomedial, and dorsal cortices, preoptic area and other parts of the hypothalamus, the limbic-related dorsomedial anterior thalamic nucleus, other parts of the subpallium, and dopaminergic neuronal populations of the midbrain. The main sets of efferent projections are to most of these sites, although a direct septo-hippocampal projection is absent. Additionally, in lizards, the septal area projects to the habenula and, as in mammals, also directly to the interpeduncular nucleus.

In birds, the connections of the septal area are generally similar to those in mammals and reptiles. One difference is the lack in birds of a direct septal projection to the interpeduncular nucleus, which is a feature shared by mammals and reptiles. A second variation is the presence of a minor septohippocampal projection in birds, which is much more prominent in mammals but altogether lacking in lizards. However, in birds, this projection arises from both the lateral and the medial septal region rather than just from the medial septal nucleus as in mammals. Also, cholinergic neurons are present in the septal region of birds, but mostly lie within the lateral nucleus rather than the medial nucleus as in mammals. Further, while the lateral septal nucleus of mammals receives amygdalar input (from its medial nucleus), similar input (from the nucleus taeniae amygdalae) is to the medial septum in birds. Thus, the individual nuclear components of the septal region in birds and mammals may be arranged differently, and while the septal region as a whole clearly is homologous across amniotes, the individual components appear to be homologous only as a set of derivatives of the septal developmental field.

EVOLUTIONARY PERSPECTIVE

A medial pallial, hippocampal area appears to be present in lampreys and all jawed vertebrates. The medial pallium that tentatively has been identified in lampreys and that is present in cartilaginous fishes is relatively small. In nonteleost ray-finned fishes, the identification of a hippocampal homologue has not been made, although topologically, it would be expected to lie within the dorsolateral pallium. Further work needs to be done on the medial pallial region of Type II sharks, skates, and/or rays to determine whether this region has any of the memory and spatial mapping functions shared by it in teleosts and amniotes.

Among teleosts, the ventral part of the lateral zone of the pallium (Dlv) in goldfish is situated in the predicted location for the hippocampus and has memory and spatial mapping functions that are strikingly like hippocampal functions in amniotes. Thus, a hippocampal formation may have become

elaborated for these functions at least twice independently—within the teleost and amniote radiations. In contrast to the cytoarchitectural features present in amniotes, however, the neurons of Dlv do not exhibit a number of the laminar and dendritic features present in the hippocampal formation of amniotes. Thus, just as is the case for the nonlimbic pallium in reptiles and birds as compared with mammals (see Chapter 25), extreme differences in cytoarchitecture, including lamination and patterns of dendritic arborization, can occur with nonetheless preservation of the capacity for similar functional processes.

A medial pallium is clearly present in amphibians and in all amniote vertebrates. The expression patterns of LIM-homeodomain genes strongly supports homology of the medial pallium of amphibians to the hippocampal formation of amniotes. The presence of a medial pallium and associated subpallial structures is thus a feature that was present in at least the ancestral stock of jawed vertebrates and may have been present in the earliest vertebrates.

MacLean, who introduced the term limbic system, hypothesized that the brain of mammals can be understood in terms of a tripartite organization that he has called the “triune brain.” As discussed in Chapter 6, he proposed that the limbic system of most extant mammals constitutes the middle of three components that were acquired progressively over evolution. According to the hypothesis, the limbic system was gained in early mammals and layered over a striatal “reptile brain.” At a later stage of mammalian evolution, the third component, the neocortical, meaning “new mammal brain,” was added. MacLean calls the limbic system the “old mammal brain.” The findings of comparative neuroanatomical investigations, as we have reviewed here, do not support the evolutionary history of the limbic system as described by the triune brain hypothesis. The present evidence indicates that the limbic system evolved long before the advent of any amniote vertebrates, let alone early mammals. Moreover, as the earliest mammals split off from the amniote stem before the earliest reptiles did, the chronology of the triune brain can hardly be considered as credible.

The limbic system is, in fact, significantly enlarged in all amniote vertebrates compared with its condition in anamniotes. In the common ancestral amniote stock, the limbic system underwent considerable enlargement and differentiation. Distinctly different parts of the medial pallium can be identified in mammals, reptiles, and birds, even though their specific homologous relationships are not yet entirely resolved. The set of components that constitute the hippocampal formation—including Ammon’s horn and the dentate gyrus and perhaps also the subiculum and entorhinal cortex—certainly appears to be homologous across amniotes as a whole entity and thus can be regarded at least as a field homology. As the most recent evidence indicates, the topology of dentate gyrus most medially to Ammon’s horn to a subicular-entorhinal region may also be common to all amniotes, with the components thus being discrete homologues. Likewise, a feed-forward trisynaptic loop type of hippocampal circuitry appears to be present in birds as well as in mammals.

A field homology may best describe the relationship of the limbic subpallium, the septal nuclei, among amniotes. The different patterns of amygdalar input and hippocampal output

between birds and mammals indicate that the septal region may be homologous as a field but without discrete, one-to-one homology of its individual nuclear components.

Another significant feature that appears unique to the hippocampal formation of amniotes is presence of the bitufted, double-pyramidal cell type. Because such neurons have not been found in any anamniote, the gain of this type of neuron probably occurred early in the stem amniote radiation. The bitufted form of dendritic ramification clearly has implications in terms of functional separation of different kinds of inputs and the subsequent processing of those inputs within the internal circuitry of the hippocampal formation of amniotes.

A marked increase in the interconnections of the limbic system and the striatal motor system may also have occurred in amniotes. The currently known interconnections of the systems are most numerous in mammals, lesser in nonmammalian amniotes, and least in anamniotes. More studies of connections are needed in anamniotes, however, to test this possibility, as the apparent trend may simply be a reflection of the relative amount of available data.

Clearly, a major change in the organization of afferent connections to the pallium occurred in ancestral amniotes. In anamniotes and particularly in amphibians, in which dorsal thalamic nuclei are in a relatively periventricular position, sensory input from the rostral part of the thalamus (i.e., the lemnothalamus) is relayed directly to the medial pallium. In amniotes, the medial pallium receives little direct sensory input. Dorsal thalamic sensory relay nuclei project predominantly to other expanded pallial areas instead, and the latter areas in turn project to the medial pallium. Thus, the medial pallium in amniotes is relatively expanded while at the same time is freed of the task of analyzing primary sensory input. Instead, the medial pallium functions at a more complex level of information analysis. In mammals, the medial pallium is the largest and most highly differentiated relative to other amniotes, and it plays a major role in learning, memory, spatial mapping, and the associated functions of motivation and emotion.

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Part Six

CONCLUSION

Evolution of Brains: A Bilaterian View

INTRODUCTION

Vertebrates constitute the largest extant radiation of chordates and likewise of the larger clade of deuterostomes to which chordates belong. Recent molecular evidence on gene expression in the developing brains of vertebrates and other chordates as well as in the developing brains of insects—particularly the fruit fly *Drosophila*—have revealed stunningly similar patterns. Thus, having surveyed in some depth the brains of vertebrates in the other chapters of this book, we will now consider vertebrate brain organization in the context of a broader view and examine, at least briefly, the brains of some of our invertebrate cousins.

The Bilateria comprise two seemingly diverse radiations, the protostomes and the deuterostomes, with chordates being a member of the latter. In this chapter, we thus will begin with a very brief overview of the protostomes, which comprise most of the invertebrate taxa, including insects, and we will discuss the organization of the nervous system in a few, selected taxa. We will focus on some of the similarities of gene expression patterns in the developing body and nervous system common to both *Drosophila* and vertebrates and their implications for the evolution of nervous systems across these highly divergent taxa.

Two basic features characterize the organization of the nervous system of Bilateria with elaborated nervous systems. The first of these features involves the regional control of cell proliferation in the radial dimension. In nonchordate invertebrates with relatively unelaborated nervous systems, neurons tend to be diffusely distributed over the body as a series of

ganglia or an interconnected nerve net, whereas in animals with elaborated nervous systems, differential regional expansion of the nervous system occurs to form a central nervous system. The second of these features involves the regional control of cell proliferation in the rostrocaudal dimension. Elaborated nervous systems are characterized by a rostral expansion, the brain. As discussed in Chapter 9, the process of further regional specification and development recently has been found to be controlled by homeobox genes. The segmental, or neuromeric, organization of the brain is a manifestation of the homeobox gene specification of regional development. As in the case of the localized formation of a nerve cord or tube, the rostrocaudal parts of the nervous system reflect localized and spatially limited increases (or decreases) in the amount of proliferation of nervous tissue.

A corollary of the feature of longitudinal differentiation of the central nervous system is the occurrence of changes that affected methods of propulsion that characterized early chordates. Whereas some nonchordate invertebrates use cilia to move their bodies through the water, locomotion in chordate invertebrates (or their larvae) is the result of waves of muscular contractions regulated by longitudinally organized nerve fibers. In the chordate invertebrate *Branchiostoma*, motor responses to stimuli are subject to control by the brain due to the rostrocaudally organized, functional differentiation of the nervous system. In chordates, as in arthropods and cephalopod molluscs, longitudinal transmission of information within the nervous system and the presence of rostrocaudally localized areas of integration and control are keystones of neural organization.

INVERTEBRATE BRAINS AND THE INVERSION HYPOTHESIS

The first multicellular animal fossils date back to approximately 700 million years ago, and the radiations of bilaterally and radially symmetrical animals diverged from each other soon thereafter. The Cambrian explosion of a multitude of invertebrate animals occurred about 550 million years ago, near the beginning of the Paleozoic era. Of the currently extant multicellular animals, some, such as Cnidaria (jellyfishes and hydra) and Ctenophora (comb jellies) are radially symmetrical, but the vast majority, the **Bilateria**, are bilaterally symmetrical. Not all members of this group are bilaterally symmetrical as

adults; for example, in many echinoderms (star fishes, sea urchins, etc.), only their larval forms are. The Bilateria are divided into two major clades, the **protostomes** and the **deuterostomes** (Fig. 31-1). These clades are distinguished by the way the gut—particularly the mouth—forms during embryological development. In protostomes, the original opening of the gastrula, the **blastopore**, forms both the mouth and the anus. In deuterostomes, a second opening (“deutero” + “stoma”) forms that becomes the mouth, while the anus forms near the region of the blastopore (see Fig. 3-2).

Based on recent studies using ribosomal DNA data, the protostomes are now divided into two groups, the **ecdysozoa** and the **lophotrochozoa** (Fig. 31-1). The ecdysozoa include arthropods—a huge group that includes insects, crustaceans

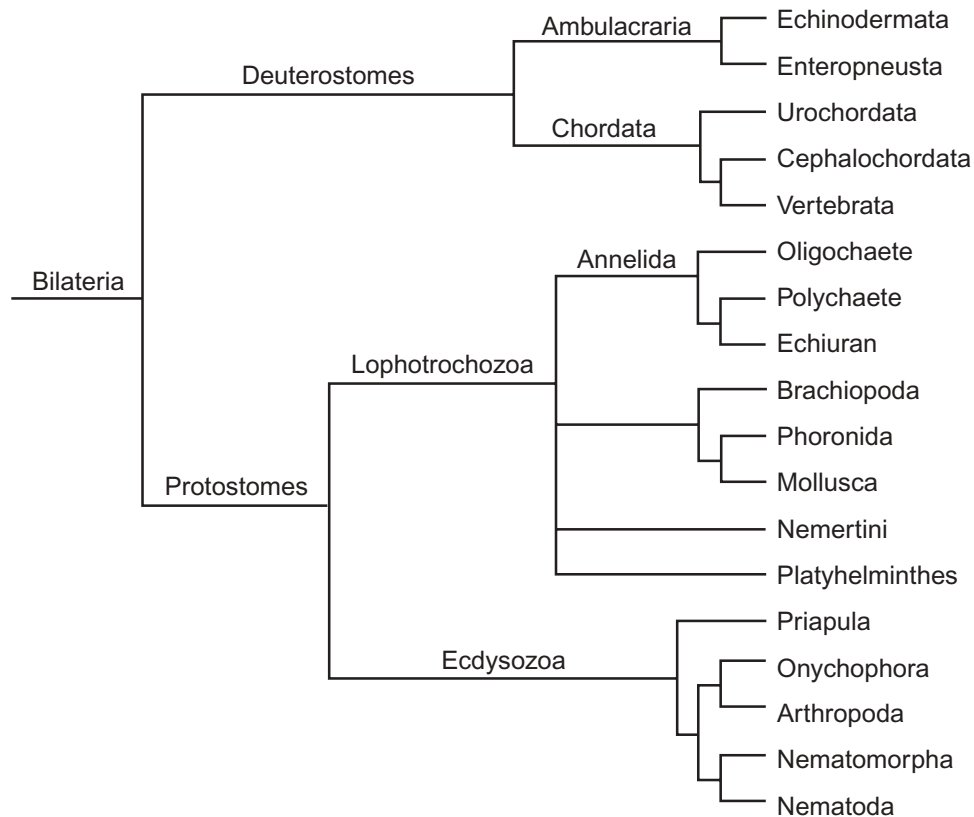


FIGURE 31-1. Dendrogram showing the relationships of most of the major taxa of Bilateria, based on Anguinaldo et al. (1997), Mallatt and Winchell (2002), Mallatt et al. (2003), and Winchell et al. (2002). [Chaetognatha and Sipuncula are not included, since their positions remain uncertain.] Three major monophyletic clades are now recognized—the Deuterostomes, Lophotrochozoa, and Ecdysozoa. Among the Lophotrochozoa, the molluscs include clams and oysters, snails, octopuses, and squid; some taxa of marine worms are represented; and the Platyhelminthes include flatworms, such as *Planaria*, and tape worms. Within the Ecdysozoa, the Arthropoda include scorpions and horseshoe crabs, as well as insects such as the fruit fly *Drosophila*. Because it is now also placed within the Ecdysozoa, the widely studied nematode *Caenorhabditis elegans* is phylogenetically much closer to *Drosophila* and other insects than previously appreciated. Within the deuterostomes (and see Fig. 31-6), a monophyletic assemblage, the Ambulacraria, comprises the Echinodermata (star fishes, sea urchins, and related taxa) and Enteropneusta (hemichordates), based on the findings of Cameron et al. (2000), Furlong and Holland (2002), and Winchell et al. (2002). The other branch of the deuterostomes is the Chordata, which comprises Urochordata (tunicates), Cephalochordata (lancelets), and the Vertebrata. It should be noted, however, that some questions persist as to whether chordates are monophyletic.

(rock lice, crabs, lobsters, shrimp, etc.) and diverse other taxa—and several other groups, including nematodes. Among the latter, the nematode *Caenorhabditis elegans* has been extensively studied as a model nervous system; the adult has exactly 302 neurons, and each can be identified and studied from individual to individual. The other major protostome clade, the lophotrochozoa, includes molluscs, various taxa of marine worms, and the Platyhelminthes. The latter includes flatworms, such as *Planaria*, and tape worms. Molluscs are a very large and diverse group. Molluscs include bivalves, such as clams and oysters; snails (gastropods); and cephalopods, such as octopuses and squid.

Large, elaborate brains (relative to body size and/or in their degree of anatomical complexity) have evolved at least once in each of the three major groups of Bilateria. In addition to the elaborate brains of vertebrates within the deuterostomes, elaborate brains also have been gained within the lophotrochozoa, particularly in the cephalopod molluscs, and within the ecdysozoa, particularly in the arthropods. As data continue to accumulate on gene expression patterns in the developing brain, the degree to which they are common to all three groups is increasingly striking. Most data are from insect developmental studies, i.e., in *Drosophila*, and vertebrate developmental studies, but the available data for molluscs are consistent with a common, shared pattern of gene expression.

Insect Brain Organization

In this brief overview, we will focus on insect brains (Fig. 31-2), since substantial genetic expression data now are available for *Drosophila*. The interested reader is urged to explore

the organization of cephalopod brains, which also are elaborated to a high degree of complexity as well as to a very large size relative to body size.

Insect brains typically comprise four large ganglia that lie at the rostral end of a nerve cord that extends the length of the body. The ganglia are called the **protocerebrum**, **deutocerebrum**, **tritocerebrum**, and **subesophageal ganglion**. **Optic lobes** and two subsequent, complex neural formations, the **medulla** and the **lamina**, form a lateral eye, one on either side, that extends out from the protocerebrum. A **hypocerebral ganglion** likewise extends from the protocerebrum. It contains neurosecretory cells, as does a more caudal ganglion, the **prothoracic ganglion**; these ganglia interact with other sets of neurosecretory cells, including some in the protocerebrum, to regulate growth, metamorphosis, and a variety of other endocrine-controlled functions. They thus exhibit multiple similarities to the hypothalamus/pituitary structures of vertebrate brains. Within the central part of the protocerebrum are a variety of neural structures, the most prominent of which is called the **mushroom body** in reference to its shape. The mushroom body is hippocampal-like in its functions of spatial mapping and memory. More caudally, the deutocerebrum receives input to its antennal lobe from the animal's antennae. The subesophageal ganglion is hindbrain-like in its control of the musculature of the mouth region and the salivary glands.

When gene expression patterns are compared between insect brains and those of vertebrates, as for the mouse (Fig. 31-3), multiple and close correspondences are observed. In the rostral part of the brain for both fly (*Drosophila*) and mouse, several homologous genes (genes of very similar molecular structure inherited from a common ancestor), including the

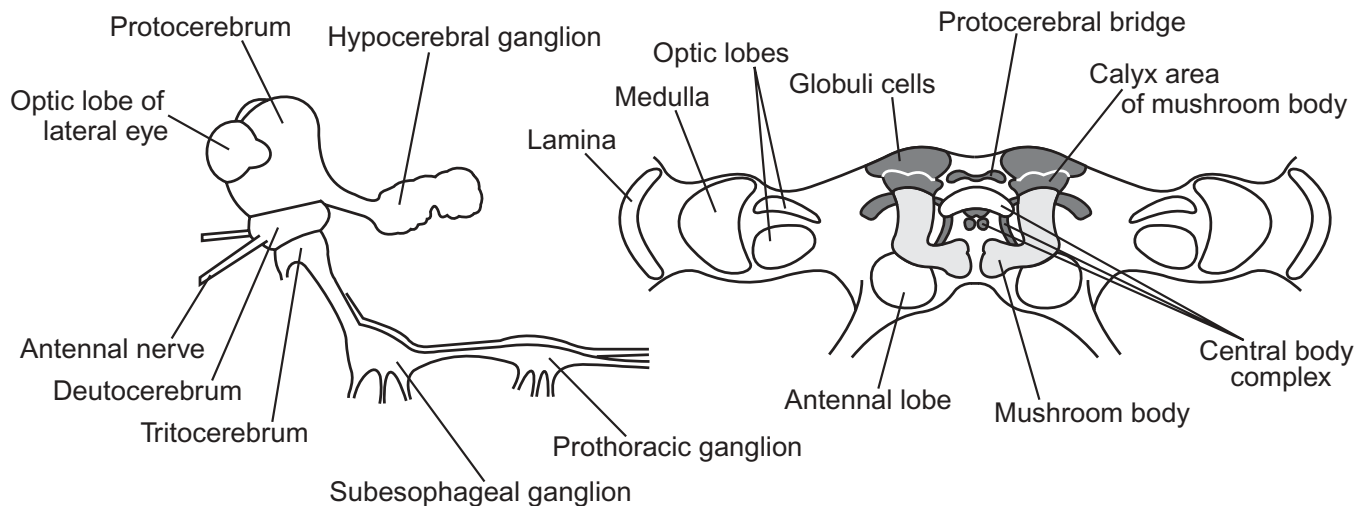


FIGURE 31-2. Arthropod brain anatomy: drawings showing a lateral view (with dorsal toward the top) of the brain of a generalized insect (left) after Brusca and Brusca (1990) and Butler (2003) and dorsal view on a larger scale of an insect brain (right) after Strausfeld (1998) and Butler (2003). In the dorsal view, only the protocerebrum (toward the top), deutocerebrum, and tritocerebrum are shown, and structures that are apomorphic for insects are darkly shaded. Lighter shading of the mushroom body, used for spatial mapping and memory functions, indicates that it may or may not be apomorphic. Drawing on left used with permission of Sinauer Associates, Inc. and that on the right with permission of S Karger AG, Basel.

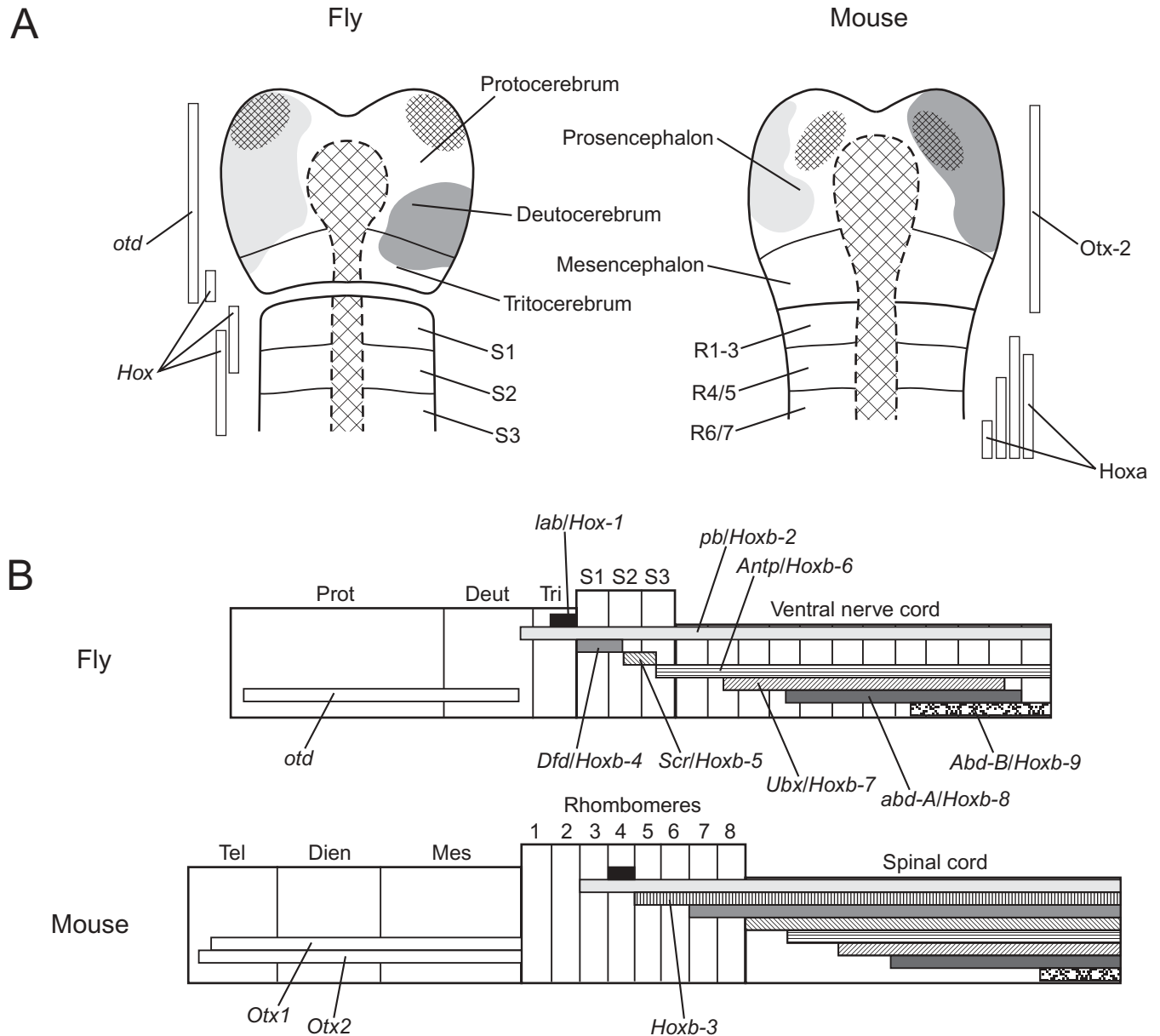


FIGURE 31-3. Comparison of gene expression patterns in the fruit fly *Drosophila* and the mouse. **A:** schematic dorsal views of the brain, with the most rostral part of the brain toward the top. In both, the homologous genes *otd/Otx-2* are expressed in the forebrain regions, whereas homologous *Hox/Hoxa* genes are expressed in the hindbrain region. Likewise, similar expression patterns occur in the forebrain regions for the homologous genes *tailless (tll/Tlx)*, indicated by light shading, and *empty spiracles (ems/Emx)*, indicated by dark shading. The eye anlagen, indicated by the smaller-scale cross-hatching, both express *Pax-6 (eyeless/Small eye)*. The medial regions, indicated by larger-scale cross-hatching, contain midline cells caudally and rostrally, the ectodermally derived stomadeum region (developing mouth opening) in the fly, and the infundibular region in the mouse. These areas shown within the larger cross-hatches all express the gene *forkhead (fkh/HNF-3 β)*. Drawings after Arendt and Nübler-Jung (1996) and used with permission of John Wiley & Sons. **B:** schematic block-diagram representation of lateral views of the brains of fly and mouse to compare gene expression patterns regionally, based on Hirth and Reichert (1999) [see also Hirth et al. (1998)]. As in A, *otd/Otx* gene expression is limited to the forebrain regions in both, and *Hox/Hoxb* family genes are expressed in the hindbrain, in the same sequence and pattern regarding the rostral-most limit of the domain for each gene. Various shading and fill patterns indicate the respective expression patterns of homologous genes in fly and mouse. Most are labeled in the fly diagram, with the fly gene given first and its vertebrate homologue indicated next. The mouse additionally has a *Hoxb-3* gene not expressed in the fly. Abbreviations (other than for genes): Deut, deutocerebrum; Dien, diencephalon; Mes, mesencephalon; Prot, protocerebrum; R1-3, R4/5, and R6/7, rhombomere segments; S1, S2, and S3, subesophageal ganglion segments; Tel, telencephalon; Tri, tritocerebrum.

orthodenticle gene(s) (*otd/Otx*), *tailless* (*tl/Tlx*), and *empty spiracles* (*ems/Emx*), are expressed (with the abbreviations in these sets designating the *Drosophila* gene first and the mouse gene second). Also, the eye anlagen express a number of homologous genes, including *Pax-6* (*eyeless/Small eye*). Thus, both anatomically and in terms of gene expression patterns, the protocerebrum-deutocerebrum-tritocerebrum complex of the fly closely resembles the forebrain (and possibly part of the midbrain) of vertebrates. Even the rostrocaudal layout is similar, with the eyes and mushroom body/hippocampus both being associated with the rostral protocerebrum/prosencephalon region. The relationship of the tritocerebrum to either caudal diencephalon or midbrain is less precise, since the midbrain may be largely an apomorphy of vertebrates.

A different set of genes, the *Hox* genes, are expressed predominantly in the insect subesophageal ganglion and, correspondingly, the homologous *Hoxa* and *Hoxb* genes are expressed in the mouse hindbrain. The expression domains of a few of the *Hox* genes in the fly extend relatively somewhat more rostrally than those of their homologues in the mouse, but the overall pattern is very consistent. As you examine Figure 31-3(B), for example, note that the most rostral limit of expression of the gene *pb/Hox-1* [these designations in the upper part of Fig. 31-3(B) being first for the fly gene and then for its mouse homologue] falls at the caudal end of the deutocerebrum, while the same gene in the mouse (*Hox-1*, indicated by similar shading in the lower part of B) has its rostral border between rhombomeres 2 and 3. Nevertheless, most *Hox/Hoxa*, *Hoxb* gene expression realms have rostral borders that lie within the hindbrain regions (subesophageal ganglion and rhombomeres, respectively) and caudally into the nerve cords in both fly and mouse, and the patterns of expression for a large number of genes are remarkably the same between these two phylogenetically distant organisms.

Urbilateria and the Ancestral Condition of Bilaterian Brains

Based on the multiple commonalities of gene expression patterns and anatomical landmarks between insect brains and vertebrates, in comparison of features present or absent from a phylogenetically wide variety of other protostome and deuterostomes, a model of the central nervous system of the earliest bilaterally symmetrical animals can be formulated. In 1996, Eddy De Robertis and Yoshiki Sasai proposed the term **Urbilateria** for these ancestral animals.

Work within the arthropod radiation, carried out by Nicholas Strausfeld, his co-workers, and others, has demonstrated that whereas some arthropods, particularly insects, have the elaborated set of structures described above, other members of this group, such as crustacea, do not exhibit all of these structures. The basic features that appear to be common to the taxon as a whole are predominantly those that correspond to parts of the diencephalon and hindbrain of vertebrates, including paired eyes, hypothalamic structures, and hindbrain motor centers. Likewise, the central nervous systems of those other invertebrate taxa that have some rostral specialization of the nerve cord, including various groups of marine worms and Platyhelminthes, predominantly exhibit the diencephalon-hindbrain components.

Using genetic and other data, Heinrich Reichert, Frank Hirth, Antonio Simeone, and others have posited the major components of the ancestral, Urbilaterian brain. This brain was tripartite, having a forebrain component, a midbrain/hindbrain boundary in the region of the deutocerebral-tritocerebral border, and a hindbrain component. Telencephalic structures would have been absent, as well as most of the midbrain region. The three major divisions of the Urbilaterian brain would have been specified by gene expression patterns similar to those for insects, vertebrates, and other bilaterally symmetrical animals, as discussed above. Paired eyes were probably also a feature of the brain in the Urbilateria, arising from the hypothalamic component of the forebrain. The eyes would have expressed the gene *Pax-6* early in their development and been simple in their anatomy, consisting either of simple **ocelli**—eye spots consisting of only one or a few photoreceptor cells—or relatively simple pigment-cup eyes, which are small formations of pigment and receptor cells. Specific features of eyes such as the ommatidia of insects and the cellular components of retinal types of eyes were evolved separately within the different radiations, consistent with their striking differences in anatomy and their downstream, unshared genetic programs.

Deuterostomes and Dorsoventral Inversion

As discussed above, the patterning genes for much of the rostrocaudal axis are highly similar across protostomes and deuterostomes. This degree of similarity extends to the patterning for the neural versus abneural axis as well—what is usually referred to as the dorsoventral axis but is in fact much better understood in terms of neural-abneural. When one compares the bodies of protostomes and deuterostomes, there appears to be an inversion of the dorsal and ventral surfaces. The brain lies rostrally in both, but while the main nerve cord of the body is situated dorsally in deuterostomes, with the gut ventral to it, it lies along the ventral aspect of the body in protostomes, with the gut dorsal to it. Until quite recently, how this difference evolved and what its significance might be has been a puzzle.

In 1822, Étienne Geoffroy Saint-Hilaire proposed homology of the ventral side of protostomes—particularly the arthropods that he studied—to the dorsal side of vertebrates. He dissected a lobster and published a meticulous sagittal drawing of it, but he oriented it such that its ventral side was to the top in order to point out the similarity thus made apparent to the vertebrate condition. This **Inversion Hypothesis** drew intense criticism and ridicule during Geoffroy Saint-Hilaire's own time, particularly from the great zoologist Georges Cuvier, and until the past decade, this idea has continued to be disparaged.

In 1996, Eddy De Robertis and Yoshiki Sasai published a summary of new molecular findings on the comparative development of the nervous system in protostomes and deuterostomes. This paper supported other recent papers by Detlev Arendt and Katharina Nübler-Jung, by Thurston Lacalli, and by several other scientists who had reached the same conclusion—that Geoffroy Saint-Hilaire had indeed been correct and that the dorsal and ventral body surfaces are reversed between protostomes and chordates. The evidence involves not only the

BOX 31-I. Eyes, Eye Evolution, and *Pax-6*

During the past decade, the pioneering work of Walter Gehring, Georg Halder, Patrick Callaerts, and their co-workers has transformed our understanding of eye evolution, and the implications of this work for shared genetic networks across the Bilateria have contributed to the virtual revolution that has taken place in the field of "evo-devo," as discussed briefly in Chapter 1. Gehring, Halder, Callaerts, and their co-workers demonstrated that expression of the gene *Pax-6* occurs in the developing eye anlagen of both mice and fruit flies. This gene is referred to as *eyeless* in *Drosophila*, *Small eye* in mice, and *Aniridia* in humans, and it is homologous across these phylogenetically highly diverse taxa. *Eyeless* can be activated ectopically on the wing of the fly, and, when it is, an ommatidial type of eye develops on the wing. Further, and remarkably, when the mouse version of the gene, *Small eye*, is activated on the fly's wing, it also is competent to induce eye formation. As in the case of *eyeless* ectopic activation, *Small eye* induces an ommatidial eye to form on the fly's wing rather than a mammalian-type retinal one. It activates the same downstream genetic cascade as *eyeless*, which is that for the ommatidial eye consistent with the fly's genetic program.

Expression of *Pax-6* has been found in a phylogenetically wide range of bilaterally symmetrical animals in conjunction with eye formation, from simple ocelli along the mantle of a clam and the small eye spots of *Planaria* (Platyhelminthes) to the morphologically highly complex eyes of cephalopods, arthropods, and vertebrates. It is one of several genes that are at or near the top of the genetic cascade for eye formation. From its wide distribution, it is clear that this gene and the several others that occur at the top of this cascade were present in the earliest bilaterally symmetrical animals. In addition to its role in eye formation, it is also expressed in the developing forebrain.

The references listed here are a sample of the literature that the interested reader can peruse and utilize to explore further this fascinating topic.

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genetically regulated morphogens used for dorsoventral patterning but also their actual functional mechanisms.

As summarized schematically in Figure 31-4, the process for induction of central nervous system tissue is highly similar between protostomes, represented by *Drosophila* on the left, and chordates, represented by vertebrates on the right. Although additional genes and processes are involved, striking similarities have been identified for at least some of them, as highlighted here. In the fly, the ectoderm expresses the *decapentaplegic* (*dpp*) gene product Dpp. Without Dpp, the

entire ectoderm would become neural tissue; Dpp suppresses the neural fate that would otherwise ensue. The mesoderm tissue produces a diffusible factor Sog, a product of the gene *short gastrulation* (*sog*). Sog acts on Dpp by blocking its receptor site, thus suppressing its suppression and allowing a neural fate for the part of the ectoderm that it affects. In protostomes, this part of the ectoderm is that which lies along the ventral surface of the adult. Sog allows neuroblasts to delaminate from the midline portion of the ventral ectoderm and then coalesce to form the neural tube. While this process of delamination is

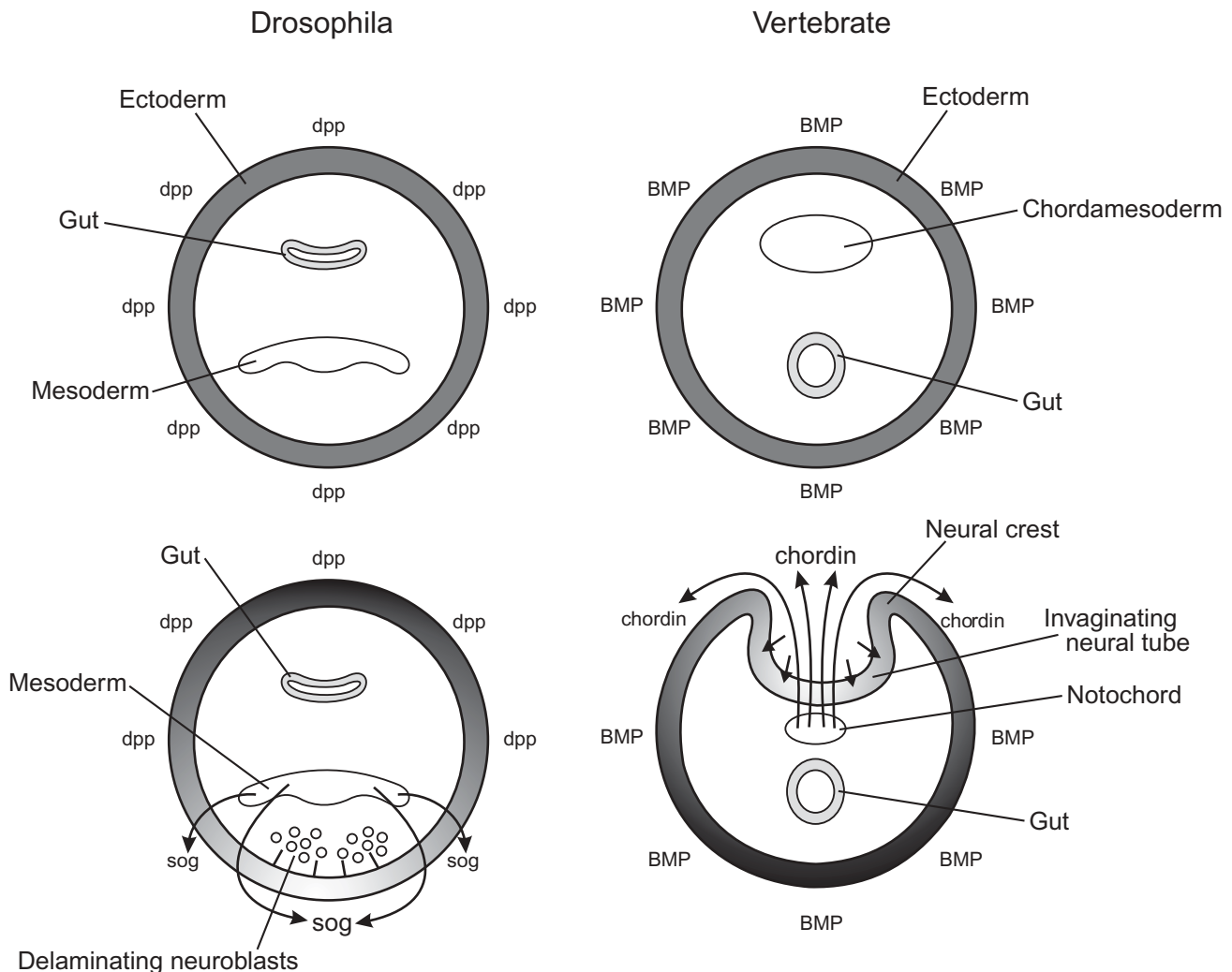


FIGURE 31-4. Comparison of neural fate determination for ectoderm in the fruit fly *Drosophila* and vertebrates. For *Drosophila*, a neural fate for the ectoderm is initially suppressed by the morphogen decapentaplegic, *dpp*. The mesoderm releases the molecule short gastrulation, *sog*, which blocks *dpp* receptor sites, allowing neuroblasts to differentiate and delaminate from the region of the ectoderm that receives the *sog* signal. Likewise in vertebrates, BMP molecules (BMP-2 and BMP-4) initially suppress neural fate for all of the ectoderm. Chordin, which is released by the underlying notochordal tissue in the dorsal midline, blocks the BMP receptor sites, allowing a neural fate for the ectoderm in this region with invagination to form the neural tube and more laterally the neural crest. Not only are the molecules homologous—*dpp* with BMP and *sog* with chordin—but their mode of action is identical. Although the dorsal-ventral axis is reversed between insects and vertebrates, the neural-abneural axis is actually the same. Diagrams based on and modified from Sanes et al. (2000) and used with permission of Elsevier.

different from that generally described for vertebrates, a similar process is also involved in the formation of the caudal part of the spinal cord in vertebrates, where, instead of the evagination process that forms most of the central nervous system (see Chapter 3), a solid neural tube forms by a condensation of neuroblasts from mesenchyme that then secondarily forms a central ventricular space—a process that is not substantially different from that for nerve cord formation in protostomes. Thus, the developmental differences of delamination in protostomes versus invagination for most of the vertebrate central nervous system are not significant in regard to the question of dorsoventral inversion.

In chordates, as shown for vertebrates in Figure 31-4, the molecular mechanism for suppression of a suppressor of neural fate is virtually the same. Two gene products, bone morphogenetic proteins 2 and 4—Bmp-2 and Bmp-4—are homologous to Dpp, and they are produced by the ectoderm. They act to suppress neural fate of the ectoderm. The morphogen chordin is produced by the mesodermal notochord tissue, and chordin is homologous to Sog. Chordin acts by blocking the Bmp receptor sites on the ectodermal cells, in the same manner as Sog does in opposing Dpp. Chordin thus allows a neural fate for the ectoderm where it is present. The neural tube forms along the midline where the concentration of chordin is greatest; the neural crest and, in the head, placodes form where the concentration is less; and the surface epithelium of the skin forms from the rest of the ectoderm where the influence of the Bmps fully prevails. The process of neurulation under the influence of chordin occurs along the midline of the dorsal surface of the body.

If vertebrates are dorsoventrally inverted protostomes, how can one reconcile the difference in the position of the neural tubes relative to that of the gut? Developmental studies, some also involving gene expression studies, have provided the likely scenario. Figure 31-5 shows a lateral view of the head of a generalized insect at the top. It shows the relationship of the central nervous system to the gut—similar to that for vertebrates with the brain dorsal to the gut but inverted in respect to the ventral nerve cord, which lies ventral to the gut. The gut actually passes through the region of the brain, encircled by the hindbrain-like subesophageal ganglion. In the bottom left part of the figure, only the brain and gut of the insect are shown, with the nerve cord extending caudally. In this rendition, however, the brain has been flipped over, so that its dorsal surface is toward the bottom.

For comparison, the brain of a vertebrate is drawn to the right, and what would be the approximate protostome position of the gut is shown by light shading. In vertebrates, the position of the mouth has changed, such that the gut no longer runs through the center of the brain but rather ends ventral to it. Essentially, the new mouth acquired in the deuterostome lineage is positioned differently from the mouth in protostomes. With the changed position of the mouth, the originally dorsal surface—the **abneural** surface—becomes the ventral surface. In other words, the neural and abneural surfaces remain the same, but the position of the mouth switches from neural in protostomes to abneural in chordates. In order to have the mouth near the substrate, where food will be found, the inversion of the ventral and dorsal surfaces occurs in chordates.

The exact point where the shift occurred is currently a matter of debate, with some, such as Claus Nielsen, pointing to the origin of chordates, as we have discussed it here, rather than including the Ambulacraria (echinoderms and enteropneust hemichordates, as discussed below). Nevertheless, the molecular evidence convincingly supports the original Inversion Hypothesis of Geoffroy Saint-Hilaire for the chordate deuterostomes. Additional support has come from recent molecular studies of the foregut: the expression of the patterning genes *brachyury* and *gooseoid* indicate that the foreguts and mouth regions of protostomes and deuterostomes are homologous, i.e., derived from the same respective structures in the common, urbilaterian ancestor. Even though the position of the mouth has changed, the foregut and mouth have maintained their homology through the diverse lineages of the Bilateria. These findings also support the notion that it is some or all of the deuterostomes that have “turned over,” rather than the common, urbilaterian ancestor having had the nerve cord dorsally and extant protostomes being the ones to have undergone the inversion.

BRAIN EVOLUTION WITHIN CHORDATES

Until recently, the origin of vertebrates from ancestral chordates was a seemingly intractable mystery. The earliest vertebrates were a group of soft-bodied deuterostomes, and, until recently, the relatively few fossils available did not provide enough information to illuminate how the transition to the earliest vertebrates occurred. Deuterostomes include two sister groups—the **Ambulacraria**, which comprise **echinoderms** and **hemichordates**, and the **Chordata** (Fig. 31-6). Due to recent molecular evidence and the phenotypic similarities of their larvae, the hemichordates and echinoderms now are placed in a monophyletic clade, the Ambulacraria, as shown in Figure 31-6. The phylum Chordata comprises the **vertebrates** and the invertebrate chordates—**urochordates (tunicates)** and **cephalochordates** (*Amphioxus*, now called *Branchiostoma*). Chordates and ambulacrarians diverged from each other more than 500 million years ago. Within the vertebrates, a lamprey is illustrated in Figure 31-6 for the cyclostomes and a **conodont** for the gnathostomes, based on the recent work of Philip Donoghue, Peter Forey, and Richard Aldridge. Conodonts, meaning “cone-tooth,” are an extinct group of chordates that were originally known only from small, cone-shaped, tooth-like fossil fragments for which they are named. It is now generally accepted that conodonts are vertebrates. More recent evidence of a mineralized dermal skeleton indicates that they may be basal for gnathostomes rather than belonging within cyclostomes.

The nervous systems of ambulacrarian deuterostomes, the echinoderms and hemichordates, do not lend many clues as to vertebrate brain origins. The echinoderms comprise starfishes, brittle stars, sea urchins and sand dollars, sea lilies and feather stars, and sea cucumbers. In all adult echinoderms, the nervous system is locally organized. No central component, such as a brain or collection of central ganglia, is present. In the worm-

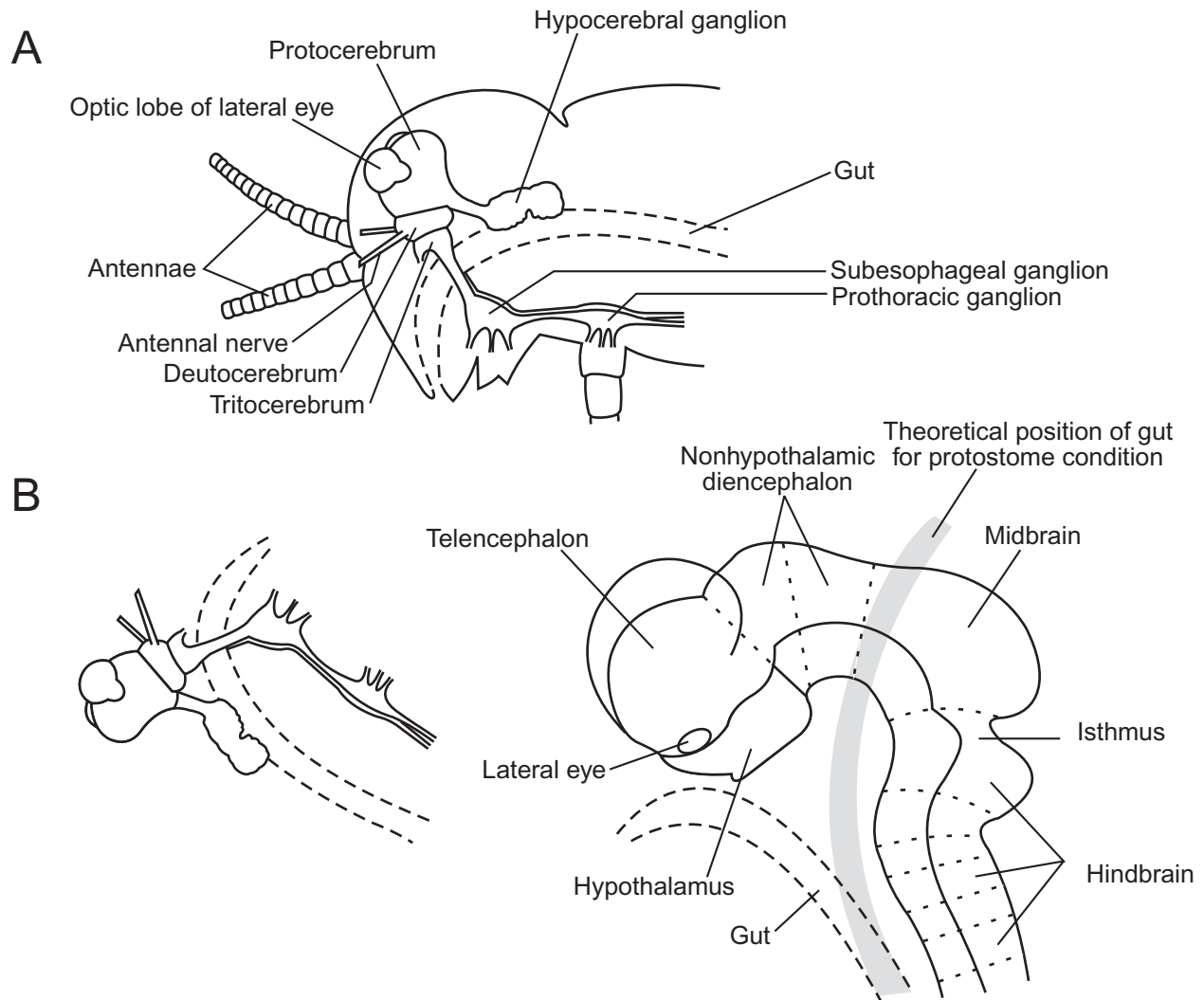


FIGURE 31-5. A: lateral view of the brain within the head of a generalized insect, showing the protostome position of the gut relative to the brain. B: comparison of the insect brain inverted, now with dorsal toward the bottom (and the gut indicated by dashed lines), on the left and a developing vertebrate brain on the right, with dorsal toward the top. For the vertebrate, the gut is shown remaining ventral to the brain throughout its course, and the theoretical position of the gut if this were an insect is shown by light shading, to illustrate the change in mouth position between protostomes and deuterostomes. As deuterostomes “turned over” in order to keep the mouth positioned toward the substrate, inversion of the dorsal-ventral axis occurred, while the neural-abneural axis remained the same. The drawing in A is after Brusca and Brusca (1990) and used with permission of Sinauer Associates, Inc. The vertebrate brain drawing in B is modified from Rubenstein and Beachy (1998) and used with permission of Elsevier.

like hemichordates, no notochord or dorsal hollow nerve cord has been identified. A nerve net is present in the epidermis and contains sensory neurons, interneurons, and some motor neurons. The nerve net is thickened to form a dorsal, solid nerve cord in the proboscis and both dorsal and ventral nerve cords in the trunk. A **neurocord**, which does have a central lumen, is formed by invaginated nervous tissue in the intermediately located collar and connects the dorsal nerve cords of the proboscis and the trunk. The neurocord contains motor neurons and interneurons and may be homologous to the

dorsal hollow nerve cord of other chordates. In the neurocord and dorsal nerve cord of the trunk is a collection of giant nerve cells, which are thought to play a role in rapid motor responses.

Among the urochordates, the larvae have the best-developed nervous systems. A **cerebral vesicle** is present in the rostral part of the body. It contains a structure called the **statocyst**, which is sensitive to gravity, and an ocellus (singular of ocelli). The cerebral vesicle is continuous with a neural tube that extends through the tail of the larva and lies dorsal to the notochord. The statocyst and ocellus are used to guide

preys left important questions unanswered as to the plesiomorphic vertebrate condition for a number of traits, not only of the brain but of the other structures of the head and body as well. In the 1990s, the findings of Thurston Lacalli and his collaborators on the developing gastrula and larvae of *Branchiostoma* dramatically increased our understanding of this cephalochordate and provided new clues as to how the brain of vertebrates evolved.

More recently, finds of early chordate fossils have increased knowledge further about early vertebrate evolution. Included in Figure 31-6 is another taxon represented here by *Haikouella lanceolatum*. As we will discuss below, the rich fossil material now available on these and several other contemporaneous chordates has provided enough information to allow a highly credible reconstruction of the steps that occurred at origin of vertebrates. The discovery and analysis of several hundred fossils of *Haikouella lanceolatum* by Jun-yuan Chen, Jon Mallatt, Nicholas Holland, and their collaborators, augmenting previously available but much less revealing material on the closely related taxa *Yunnanzoon lividum*, have allowed for an almost complete picture of the transition to the earliest vertebrates to be formulated.

Some previous models of the earliest vertebrates had been constructed from the recognized plesiomorphic features for living vertebrate groups. The earliest vertebrates were predicted to be small animals of a fish-like shape with a series of gill slits in the pharynx and segmental body musculature. They

would have moved through the water as the result of alternating waves of muscle contractions. These animals had a notochord, derived from the roof of the archenteron (the primitive gut), which is formed during gastrulation, and a dorsal hollow nerve cord. The nerve cord was expanded at its rostral end. Sensory receptive structures for senses including terminal and/or olfactory, visual (retinal photoreceptive), pineal-parapineal photoreceptive, taste, ocataval, and lateral line were gained relatively early in the vertebrate lineage, but whether or not they all were gained simultaneously was disputed. Finally, whereas in invertebrates, elaboration of the nervous system is at least partly accomplished by increasing the degree of complexity of individual neurons, elaboration of the nervous system in the earliest vertebrates was characterized by a marked increase in the number of neurons. Until the most recent finds and analysis of early fossil chordates, the cephalochordate *Branchiostoma* most closely resembled this model, still differing, however, in several key features.

In larval lancelets, the cephalochordate *Branchiostoma*, a **dorsal hollow nerve cord** is present dorsal to the notochord and can be divided into a dorsolateral sensory zone and a ventral motor zone. Ocelli, which are each formed by only one receptor cell and one pigmented cell, are distributed along the dorsal nerve cord. The rostral end of the nerve cord contains an expanded portion formed by ciliated cells, the **cerebral vesicle**, as shown in Figure 31-7. An enlarged view of the cerebral vesicle is shown in Figure 31-8(C). A cluster of photore-

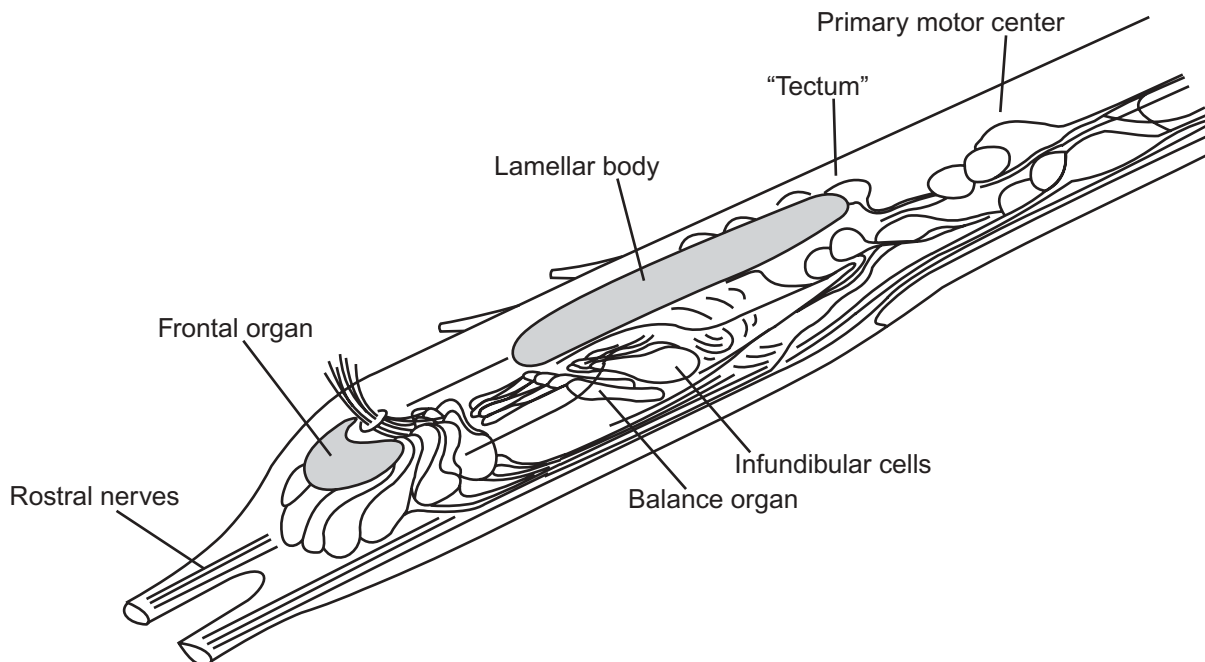


FIGURE 31-7. Semischematic drawing of a dorsolateral view of the cerebral vesicle, tectum, and primary motor center, which lie at the anterior end of a 12.5-day-old lancelet larva. Components of the cerebral vesicle include the frontal organ, or eye, with its pigment spot, a so-called balance organ that is in fact part of the hypothalamus, infundibular cells, and the lamellar body. The so-called tectum may or may not be comparable to that of vertebrate midbrains, but large motor cells that lie caudally and comprise a primary motor center are probably homologous to the vertebrate hindbrain. Redrawn from Lacalli (1996b) and used with permission of the Royal Society of London.

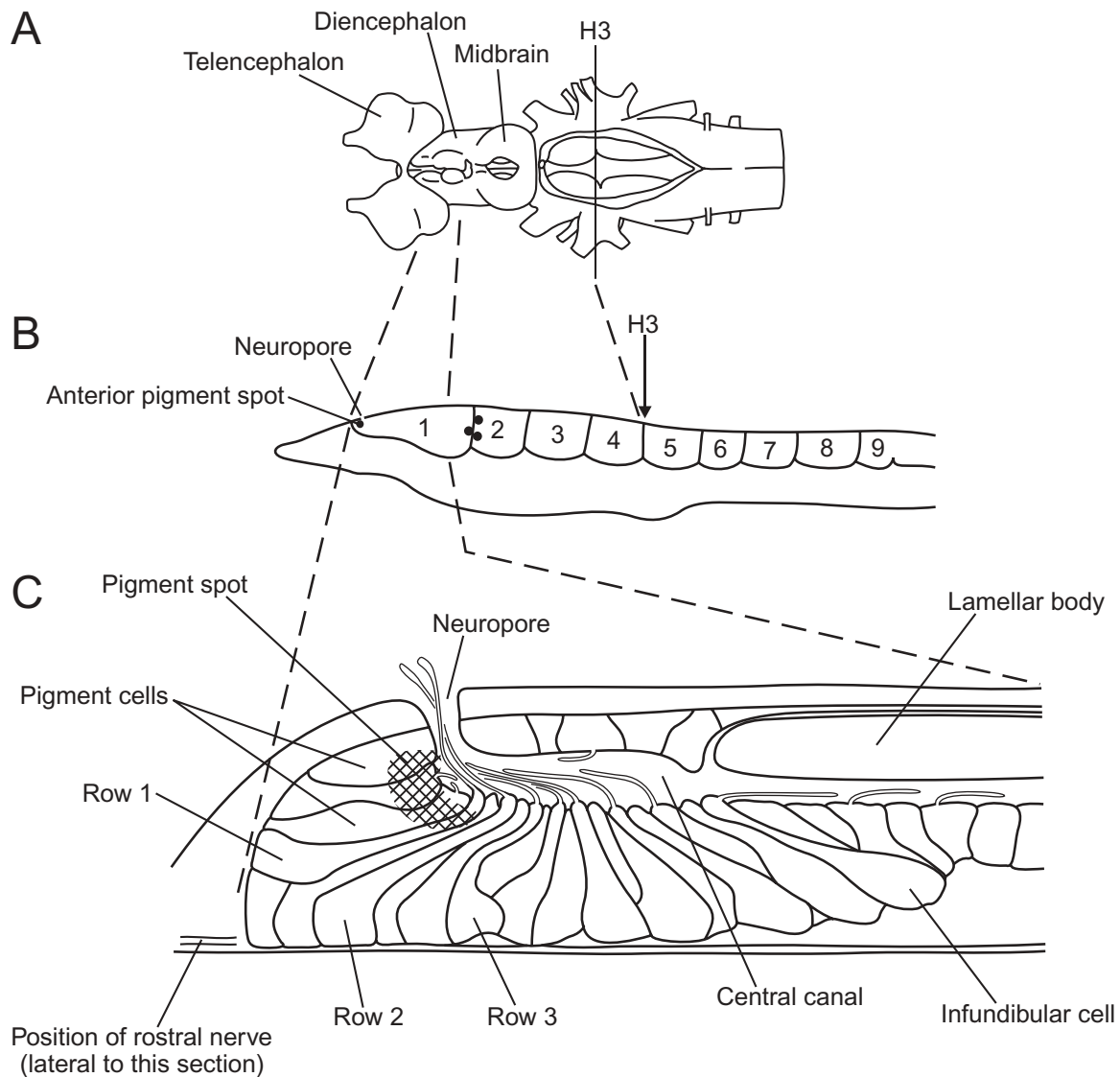


FIGURE 31-8. Drawing of a dorsal view of a lamprey brain (A), showing the position of the rostral expression limit of Hox-3 (H3), and compared with a lateral view of the rostral part of the body with somites, numbered 1–9 in a lancelet larvae (B) and an enlarged, lateral view of the cerebral vesicle of the lancelet larvae (C). Dashed lines between the drawings indicate comparable landmarks and portions of the animals. In B, the set of large, hindbrain motor neurons are indicated by three black dots and the rostral limit of Hox-3 expression by H3. In C, rows of anterior cells are labeled Row 1, 2, and 3, which are part of the frontal eye. The cells in rows 1 and 2 are flask-shaped and may be receptor cells, whereas those of row 3 are more neuron-like. A adapted from Northcutt and Puzdrowski (1988) and used with permission of S Karger AG, Basel. B and C adapted from Lacalli et al. (1994) and used with permission of the Royal Society of London.

ceptive, pigment-containing cells and associated flask-shaped and nerve-like cells, called the **frontal organ**, or **frontal eye**, lies at the rostral end of the cerebral vesicle. The cerebral vesicle contains a **central canal** that opens to the surface through a **neuropore**. Caudal to the neuropore, the dorsal roof of the posterior part of the cerebral vesicle contains cells with cilia that produce stacks of lamellae and may also be photoreceptive; this set of cells is known as the **lamellar body**.

At the junction between the posterior and anterior parts of the cerebral vesicle are a **balance organ** and a cluster of **infundibular cells** in the ventral part of the vesicle. The infundibular cells secrete a noncellular strand called **Reissner's fiber**, which extends down the central canal. A pair of **rostral nerves** arises from within the cerebral vesicle, and a segmented series of **dorsal and ventral spinal nerves** arises from the dorsal nerve cord.

Lacalli proposed putative homology of a number of these features in the larval lancelet with various structures in vertebrate brains, which has been supported by more recent work. Due to multiple structural and histochemical similarities, the unpaired frontal eye of *Branchiostoma* appears to be homologous to the retinas of the paired eyes of vertebrates. The balance organ is a putative homologue of at least part of the vertebrate hypothalamus. The infundibular cells appear to be homologous to the infundibulum of vertebrates; infundibular cells in embryonic fish occupy the same position and also secrete a Reissner's fiber. The lamellar body appears to be the homologue of the vertebrate pineal-parapineal complex, due to positional and ultrastructural similarities. The rostral nerves may be homologues of the terminal and/or olfactory nerves, but additional study of them needs to be done.

Thus, the cerebral vesicle contains structures that appear to be homologues of the vertebrate paired retinas, hypothalamus, infundibulum, and pineal-parapineal complex, all of which lie within or are derived from the diencephalon. The cerebral vesicle therefore appears to be homologous to the vertebrate diencephalon, with perhaps a small telencephalic component rostrally. Immediately caudal to the cerebral vesicle are several large ventral motor neurons [Fig. 31-8(B)]. Lacalli postulated that these may be homologous to the anterior-most of the ventral motor neurons in vertebrates, that is, the oculomotor neurons that innervate the muscles of the eye. If this comparison is correct, the region in which these ventral motor neurons lie in *Branchiostoma* would be the homologue to at least part of the vertebrate midbrain.

The somites in *Branchiostoma* and their possible correspondence to somitomeres and somites in vertebrates (see Chapter 9) are consistent with the above proposed homologies for the rostral components of the central nervous system. Peter Holland and his collaborators determined the location of the rostral expression border of the homeobox gene *AmphiHox 3*, indicated by H3 in Figure 31-8(B) for *Branchiostoma*, which appears to be a homologue of the *Hox* paralog group 3 (H3) in vertebrates, as shown with its rostral border positioned within the hindbrain of the lamprey in Figure 31-8(A).

The cerebral vesicle in *Branchiostoma* is aligned with the first somite and, as noted above, appears to be a diencephalic homologue, with perhaps a small telencephalic component. No somitomere is present in vertebrates that would correspond to the first somite in *Branchiostoma*; whether a corresponding somitic entity was present in the common ancestral stock of cephalochordates and vertebrates is unknown. If the anterior-most ventral motor neurons in *Branchiostoma* [indicated by the large dots in Fig. 31-8(B)] are homologues of vertebrate oculomotor neurons, and particularly of the neurons of cranial nerve III, then the rostral end of the midbrain in *Branchiostoma* would be aligned with the rostral end of its second somite, which would then correspond to the rostral end of the first head segment and the somitomeric region in vertebrates. The position of the rostral expression limit of *Hox-3* is at the caudal border of the fourth somite. Thus, somites 2, 3, and 4 would correspond to the somitomeric part of the head in vertebrates that comprises the first three head segments and encompasses the three oculomotor cranial nerves.

By comparing the putative homologues of parts of the brain present in *Branchiostoma* with the brain in vertebrates,

some of the features of the brain in the common ancestral stock of cephalochordates and vertebrates were posited. The brain of the common ancestor might have had the four basic divisions of the central nervous system: forebrain, midbrain, hindbrain, and spinal cord. However, as discussed below, most of the midbrain region may be apomorphic to definitive vertebrates. A diencephalon would have been present, with at least a retinal apparatus, a hypothalamus, an infundibulum, and a photoreceptive pineal-parapineal complex. The rostral extent of ventral motor neurons would have marked the rostral border of the midbrain. Some features remained mysterious, however. Whether a telencephalic component was present in the forebrain, other than a small number of neurons in receipt of the rostral or terminal/olfactory nerve input, could not be determined from the *Branchiostoma* comparison alone. Whether the retinal apparatus was paired or unpaired could not be determined, and whether the notochord would have extended rostral to the rostral border of the brain, as it does in *Branchiostoma*, or have ended caudal to the level of the forebrain, as it does in vertebrates, could not be determined. Also undetermined was how a common ancestor of this type gave rise to the vertebrate radiation—a transition that involved changes in multiple structures and for multiple systems.

THE ORIGIN OF VERTEBRATES

Among chordates, vertebrates are uniquely characterized by a constellation of features that include paired, lateral eyes, a relatively large brain/body ratio, and marked elaboration of two ectodermal tissues—neural crest and neurogenic placodes—which directly give rise to or are crucial for the development of the peripheral sensory neurons for olfaction, somatosensory innervation of the head, taste, hearing, and the lateral line system, the postganglionic motor neurons of the autonomic nervous system, most of the skull including the sensory capsules for the eyes and ears, and a variety of other tissues including the visceral arches (mandibular, hyoid, and branchial). In vertebrate embryos, neural crest and neurogenic placode tissues arise lateral to the developing neural tube, where, as discussed above, the gradient of chordin decreases in a mediolateral direction. Whether all of the components of this constellation of features were gained simultaneously in the earliest vertebrates or were gained separately in a serial manner has been debated.

Recognizing the importance of neural crest and neurogenic placodes in vertebrate evolution, Glenn Northcutt and Carl Gans had proposed that elaboration of these tissues was the seminal event for the origin of vertebrates and that these tissues became elaborated at the same time as the enlarged brain and paired eyes were gained. In their model, the enlarged brain, paired eyes, and all or most of the neural crest/placodal sensory systems of the head and body, as well as the other neural crest derivatives such as the skull and sensory capsules were gained simultaneously. Northcutt and Gans also posited that changes in the pharynx allowed a change from ciliary to muscular ventilation, involving the branchial arch musculature, and that this change preceded a change from suspension feeding to predation. Based on fossil evidence available in the early to mid-1990s, before the discovery of *Haikouella*, Jon

Mallatt proposed a reconstruction of the earliest, ancestral vertebrate that included the neural crest-derived branchial bars, skull, and dermal scales, an oral ring with tentacles at the mouth opening, and central nervous system features that included paired eyes and an enlarged brain, the latter including a telencephalon. Mallatt's model is shown in Figure 31-9(A).

In early 1999, while the first *Haikouella* specimens were being found and analyzed, Ann Butler posited a model of the transitional, earliest vertebrate form based on Lacalli's cephalo-chordate findings, fossil material described in the literature, and an intuition that a transitional condition had occurred rather than a simultaneous elaboration of both the central nervous system (paired eyes and brain) and the peripheral nervous system, skull, and other neural crest and placode derivatives. Convincing evidence for paired eyes had not been found in fossils of early chordate material (such as conodonts and two other taxa, *Pikaia* and *Yunnanozoon*) at that time. However, Butler reasoned that if vertebrates had a transitional origin in terms of the nervous system, elaboration of the peripheral nervous sensory systems without concurrent elaboration of the spinal cord and brain would not provide any adaptive advantage. Greatly augmented sensory information without the central capacity to analyze it would not be of significant value. If, on the other hand, the brain became enlarged first, the paired eyes that are part of the brain rather than peripheral nervous structures could provide augmented sensory input at the same time that the enlarged brain could process it to some adaptive advantage. Based on this idea of initial elaboration of the brain and paired eyes, she termed this model [Fig. 31-10(A)] a "cephalate."

Haikouella

Subsequent to these various models of the transition to vertebrates, the analysis of over 300 fossils of the chordate *Haikouella lanceolatum* by Jun-yuan Chen, Jon Mallatt, and their collaborators has illuminated the origin of vertebrates from the invertebrate chordate lineage. The name for the genus *Haikouella* was derived from the location of its discovery in Haikou, China, and the specific name *lanceolatum* was derived from its lancelet shape. Most fossil specimens of adult *Haikouella* are 25–30 mm in length, and many features can be identified that are shared with vertebrates. Some prominent vertebrate features are clearly absent from *Haikouella*, however, clearly establishing it as a protovertebrate, transitional form.

Of particular importance for understanding the transition to vertebrates, *Haikouella* fossils exhibit paired eyes. This condition contrasts with the single, midline, cyclopic frontal eye present in *Branchiostoma*. In vertebrates and thus probably also in *Haikouella*, the morphogen produced by the patterning gene *Sonic hedgehog*, Shh, and released from the prechordal mesoderm, called the prechordal plate, is necessary to implement splitting of the originally single, midline optic stalk into paired protrusions that form the lateral eye. The morphogen appears to act by suppressing *Pax-6* expression in the midline, resulting in a split of the originally single eye anlage. Mice lacking the *Sonic hedgehog* gene exhibit multiple defects, including a cyclopic condition of the eye. Lack of *Pax-6* function but with apparent preservation of *Sonic hedgehog* function results in a different type of pathology: in the medaka (*Oryzias latipes*), a euteleost fish, individuals that are bred as

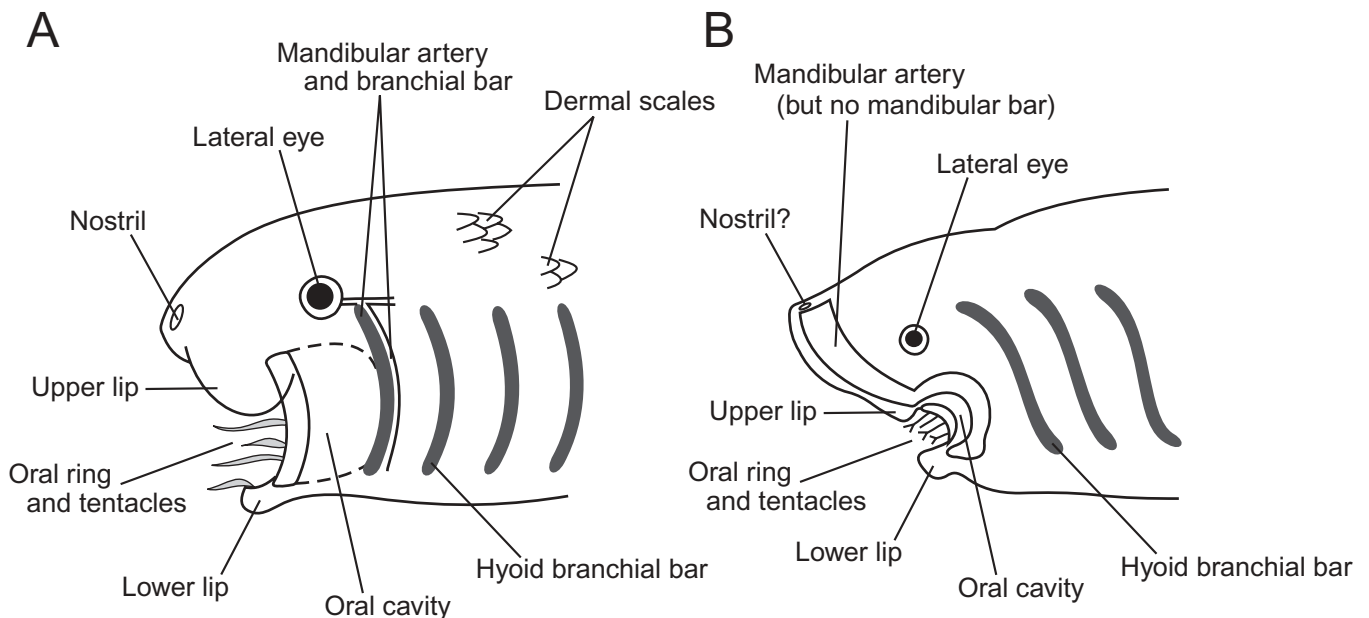


FIGURE 31-9. Reconstruction (A) from Mallet (1996) of the head of his predicted ancestor of all living vertebrates (craniates) compared with actual drawing of *Haikouella*'s head region (B). Adapted from Mallatt and Chen (2003) and used with permission of John Wiley & Sons. The similarity of the external anatomy is striking on most points.

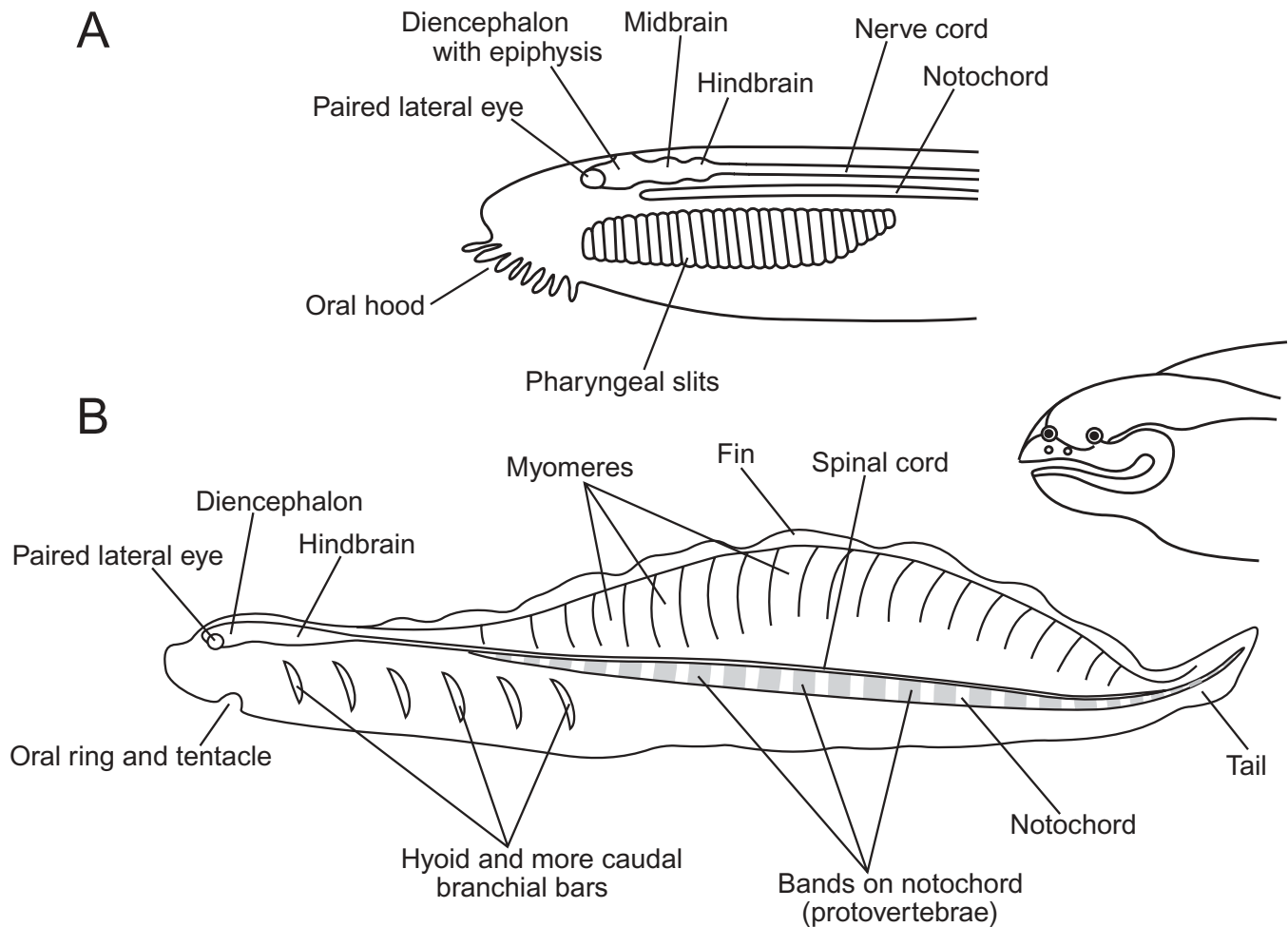


FIGURE 31-10. Reconstruction (A) from Butler (2000) of the head of her predicted ancestor of all living vertebrates, which she termed a cephalate, compared with a drawing of *Haikouella* (B), with an inset of the head (at the upper right) showing a more frontal view that includes both lateral eyes and possibly small paired nostrils. Butler's prediction of the paired eyes and brain being gained before the elaboration of neural crest and neurogenic placodes is strongly supported by the evidence from *Haikouella*. Paired eyes are clearly present, and the brain-body ratio appears comparable to that of a lamprey. This animal had a few neural crest derivatives, including most of the branchial bars, but it lacked most neural crest and neurogenic placodal derivatives, including a skull, bony orbits, ears, a nose, and dermal scales. Also, the telencephalon, which appears to require an olfactory placode for its induction, is small to absent in *Haikouella*, as are any putative olfactory structures. Butler also correctly predicted that the notochord did not extend all the way rostrally as it does in lancelets. *Haikouella* drawings based on Mallatt and Chen (2003). All parts of this figure used with permission of John Wiley & Sons.

homozygous for the *eyeless* mutation exhibit multiple abnormalities, including anophthalmia, i.e., the lack of eyes. In these fishes, the developmental relationship of the eyes and the hypothalamus is clearly apparent, since they have retinal-like structures that develop within the preoptic/hypothalamic region of the brain and remain there rather than evaginating in the normal manner. These retinal structures are present bilaterally, tending to be juxtaposed and/or fused across the midline within the third ventricle. Thus, in *Haikouella*, as in definitive vertebrates, both *Pax-6* and *Sonic hedgehog* would have participated in the development of the paired, lateral eyes.

Haikouella also exhibits some but not many neural crest derivatives. A comparison of Mallatt's original model of the deeply ancestral vertebrate with the head of *Haikouella* (Fig. 31-10) shows both with the lateral eye present, the oral ring with tentacles and upper and lower lips, possibly a small nostril, and most of the neural crest-derived branchial bars. However, *Haikouella* lacked the mandibular branchial bar. It also lacked the neural crest-derived skull and dermal scales that characterize vertebrates. *Haikouella* fossils also lack any indication of an ear or lateral line system. Although *Haikouella* thus lacked many of the internal, bony features that character-

ize extant vertebrates, Mallatt's original model was stunningly close in most of its external features to the actual *Haikouella* specimens.

Fortunately, the fossil material on *Haikouella* is rich and extensive enough to reveal a number of details about the internal anatomy, including that of the central nervous system. As shown in Figure 31-10(B), consistent with the predictions of Butler's cephalate model, *Haikouella* had a significantly enlarged brain in addition to its paired lateral eyes (both of the latter shown in the inset drawing of a fortuitous fossil find that clearly reveals a bilateral pair of eyes). However, *Haikouella* apparently lacked most of the neural crest-derived bony and peripheral nervous system components predicted by other models. Mallatt and Chen noted that the size of the brain of *Haikouella* in relation to its body size is on a par with that of extant lampreys and far exceeds that of *Branchiostoma*. A telencephalon is mostly or totally absent in *Haikouella*, however, again as predicted by the cephalate model. While a small nostril and a small telencephalic component of the forebrain may have been present, the fossils reveal that the brain consisted predominantly of a diencephalon, a transitional area marked by an indentation, and a hindbrain.

A further point of similarity with the cephalate model is that the notochord does not extend all the way to the rostrum of the animal but ends caudal to the rostral part of the central nervous system. The position of the rostral end of the notochord in the cephalate model had been based on fossil evidence from other early chordates—*Pikaia* and similar fossil taxa. In fact, in *Haikouella*, the rostral end of the notochord appears to lie even farther caudally than that of either the cephalate model or extant vertebrates. In this regard, it is interesting to note again the likely correlation of the presence of prechordal mesoderm in both *Haikouella* and vertebrates, rather than notochordal tissue, ventral to the rostral part of the brain and the occurrence of paired lateral eyes, likely due to *Sonic hedgehog* activity of the prechordal mesoderm in both. Although the notochord also produces Shh, the correlation of prechordal mesoderm with the presence of paired eyes may be significant. Additionally of interest is the presence of bar-like indications along the notochord [Fig. 31-10(B)], which Mallatt and Chen interpret as protovertebrae. These bars further support the position of *Haikouella* as a basal, ancestral, transitional form to the vertebrate radiation.

The *Haikouella* material thus has proven to be a treasure-trove of exceptional significance. The *Haikouella* fossil evidence supports the hypothesis of Northcutt and Gans that muscular ventilation with the branchial musculature replaced ciliary ventilation before the evolution of predatory feeding. It supports the shape of the head and multiple external features as envisioned by Mallatt. In terms of nervous system evolution, it supports the cephalate model of Butler in that the paired eyes and brain, the latter lacking all or most of the telencephalon, were enlarged and elaborated before most neural crest- and placode-derived structures were gained and a definitive telencephalon was acquired. The importance of neural crest in this early transition cannot be underestimated in terms of the respiratory gain allowed by the branchial bar musculature. The elaboration of the paired eyes and brain before most or all of the neural crest- and placode-derived peripheral nervous

system, as predicted by the cephalate model and present in *Haikouella*, allowed an adaptive transition on the path to the full-blown vertebrate condition.

Sensory System Evolution in the Vertebrate Lineage

Within the vertebrate lineage, subsequent to *Haikouella* and with substantially more extensive elaboration of neural crest and neurogenic placodes, we can postulate that the earliest definitive vertebrates would have had a telencephalon, with a pair of rostral nerves terminating in it. The identity of these nerves as either olfactory or terminal cannot be determined presently, but olfactory is the more probable alternative. Although paired olfactory nerves are present in all extant vertebrate groups, paired terminal nerves with GnRH-positive (gonadotropin hormone releasing hormone) neurons are present only in jawed vertebrates; terminal nerve-like neurons are present in lampreys but do not contain GnRH, and a terminal nerve has not been found in hagfishes. Determination of the identity of the rostral nerves in *Branchiostoma* will help to clarify this issue.

Paired eyes were present in the earliest vertebrates. Although *Branchiostoma* has the single, cyclopic type of frontal eye, paired eyes occur in many invertebrates, and the *Haikouella* fossil material convincingly establishes them as ancestral for vertebrates. The cyclopic condition in *Branchiostoma* is thus most likely an apomorphy of cephalochordates.

Structures associated with the retina in vertebrates, such as the cornea, lens, and iris, are present in lampreys and jawed vertebrates but absent in hagfishes and in all invertebrate chordates. Likewise, no evidence for such structures has been found in the *Haikouella* fossils. Thus, they may have evolved subsequent to the transitional *Haikouella*-like stage. Extraocular eye muscles and their cranial nerves are also present among extant vertebrates in the same distribution. Fossil evidence indicates the presence of these muscles and nerves in fossils of osteostracans, and the presence of neurons in the brain of *Branchiostoma* that are the putative homologues of vertebrate oculomotor neurons raises the possibility that muscles associated with the retinal apparatus and their innervating ventral motor neurons were present in the earliest vertebrates and have subsequently been lost in hagfishes. The same may well be true for the cornea, lens, and iris. As discussed in Chapter 4 (see Box 4-1), recent molecular evidence supports the inclusion of hagfishes within the vertebrate radiation. Their lack of vertebrae is now regarded as an apomorphy within this taxon, along with the absence (hypothesized loss) of a number of nervous system and related features as listed in this section.

The earliest vertebrates had an unpaired, median, pineal-parapineal photoreceptor apparatus in the roof of the diencephalon. A pineal-parapineal complex is plesiomorphic for jawed vertebrates. Furthermore, this structure is present in lampreys and absent in hagfishes, and the putatively homologous lamellar body is present in *Branchiostoma*. This distribution suggests that a pineal-parapineal apparatus is plesiomorphic for at least the common ancestral stock of cephalochordates and vertebrates, and its absence in hagfishes is an apomorphy.

The neural crest- and placode-derived components of the peripheral nervous system were gained early in the vertebrate lineage if not at its inception. No evidence for the lateral line senses of electroreception and mechanoreception has been found in invertebrate chordates (although sensory papillae that detect vibrations and/or water flow are present in the invertebrate chaetognaths) or in *Haikouella* fossils. The placodal tissue for both lateral line senses may have evolved in conjunction with the early vertebrate feature of the deposition of calcium salts in the dentine, which enhance electroreception. Furthermore, depressions and canal systems that could have effectively shielded lateral line electroreceptors have been found in the earliest fishes known from the fossil record. Such shielding is essential for perceiving the direction of the stimulus source. Extant hagfishes appear to lack electroreception and thus may have lost the apparatus for it over the course of their evolution. Otic organs for vestibular sense and hearing characterize all major groups of living vertebrates, even though not all components, such as horizontal semicircular canals, are present in all vertebrates. Similarly, the chemosensory system of taste and the profundal and trigeminal sensory systems are common features of vertebrates. With the exception of possible rostral sensory nerves in *Branchiostoma*, no such organs are evident in either extant *Branchiostoma* or in *Haikouella* fossils.

Organization of the Vertebrate Brain

With the full elaboration of neural crest and placodes, the major divisions of forebrain, midbrain, hindbrain, and spinal cord were present quite early in vertebrate evolution. At this stage, all of the major nonvisual sensory and motor systems organized for active propulsion and predation were gained.

The earliest definitive vertebrates, following the transitional *Haikouella*-like stage, would very probably have had an expanded telencephalon due to the influence of placodal tissue. The presence of paired olfactory organs that are connected to the forebrain appears to be necessary for the development of normal telencephalic lobes. The neural plate cells that give rise to the definitive telencephalon seem to require the influence of olfactory placodal tissue to develop normally. With the development of the olfactory inputs to the telencephalon, the presence of an olfactory pallium, as is present in extant vertebrates, can be postulated for the early definitive vertebrates. That the entire pallium was olfactory in the earliest vertebrates (as it is in hagfishes) is probable, with olfactory projections being limited to the lateral pallial region only in gnathostomes.

Most of the neuron cell bodies in the brains of these early vertebrates would have been in a periventricular position, rather than migrated laterally (centrifugally) within the various parts of the brain. As do other parts of the brain, the telencephalon varies markedly within each of the four major vertebrate radiations in the degree of neuronal migration and elaboration, as summarized here in Figure 31-11 (and see Chapter 4). Type I brains, with relatively little migration of neuronal cell bodies away from the generative ventricular zone, occur in lampreys, squalomorph sharks, cladistian and some other ray-finned fishes, and in lungfishes, coelacanth, and amphibians. In contrast, Type II brains, with extensive neuronal

proliferation and migration, occur in hagfishes, galeomorph sharks, skates and rays, teleost fishes, and tetrapods. Based on brain-body ratios, the earliest definitive vertebrates would have exhibited Type I brains, such as that in extant lampreys and most likely in the similarly scaled brain of *Haikouella*.

In all vertebrates, a diencephalon is present that contains a hypothalamus and infundibulum and also gives rise to the paired neural retinas. A diencephalon with these structures can also be recognized in cephalochordates and is thus plesiomorphic for the common ancestor of cephalochordates and vertebrates. A pineal-parapineal apparatus is present in all vertebrates except hagfishes and is present in *Branchiostoma*. This feature of the diencephalon is thus also plesiomorphic for the common ancestor of cephalochordates and vertebrates. Other portions of the diencephalon appear to be unique to vertebrates. These include an epithalamus with paired, asymmetrical habenulae, a dorsal thalamus, and probably a ventral thalamus.

In jawed vertebrates, the dorsal thalamus is composed of two divisions: the lemnothalamus and the collothalamus. A nucleus anterior that may constitute the lemnothalamus has been identified in both lampreys and hagfishes, but further study of the dorsal thalamus of lampreys and hagfishes is needed to determine whether the two divisions were plesiomorphic for all vertebrates. However this question is resolved, a lemnothalamus-medial pallium system may have been one of the earliest ascending systems established to the telencephalic pallium. A striatal area in the telencephalon has been identified in both lampreys and hagfishes, implying that the striatum is plesiomorphic for vertebrates; thus, a collothalamus relaying visual and other sensory information from the roof of the midbrain to the striatum also may have been present in the earliest definitive vertebrates. Finally, the possible presence of cell groups homologous to the preglomerular nuclear complex in the caudal diencephalon of jawless vertebrates remains to be investigated, but the presence of receptors for the senses of taste and lateral line mechanoreception (and electroreception in lampreys) in these vertebrates suggests that cell groups relaying ascending information from these systems may have been present early in vertebrate history.

A midbrain containing both a roof (tectum) and a tegmental region is plesiomorphic for vertebrates. The only putatively homologous part of the midbrain yet identified in *Branchiostoma* is the ventral motor cells. Likewise, the brain in *Haikouella* appears to have diencephalic and hindbrain divisions but only a sulcal transition area in between. The midbrain sensory roof thus may be unique to vertebrates. Consistent with this idea, the gene *AmphiEvxA* is not expressed at the putative midbrain-hindbrain boundary—the region of the isthmus—in *Branchiostoma*, while its two vertebrate homologues, the *Evx1* and *Evx2* genes, are expressed in this region and contribute to the establishment of the midbrain-hindbrain boundary.

The hindbrain is smaller in hagfishes than in lampreys and jawed vertebrates, and fossil evidence suggests that it was small plesiomorphically for vertebrates. As the lateral line and octaval sensory receptors and bipolar cells evolved with the elaboration of their placodes, they can be postulated to have entered the hindbrain and synapsed in a localized region within it. This

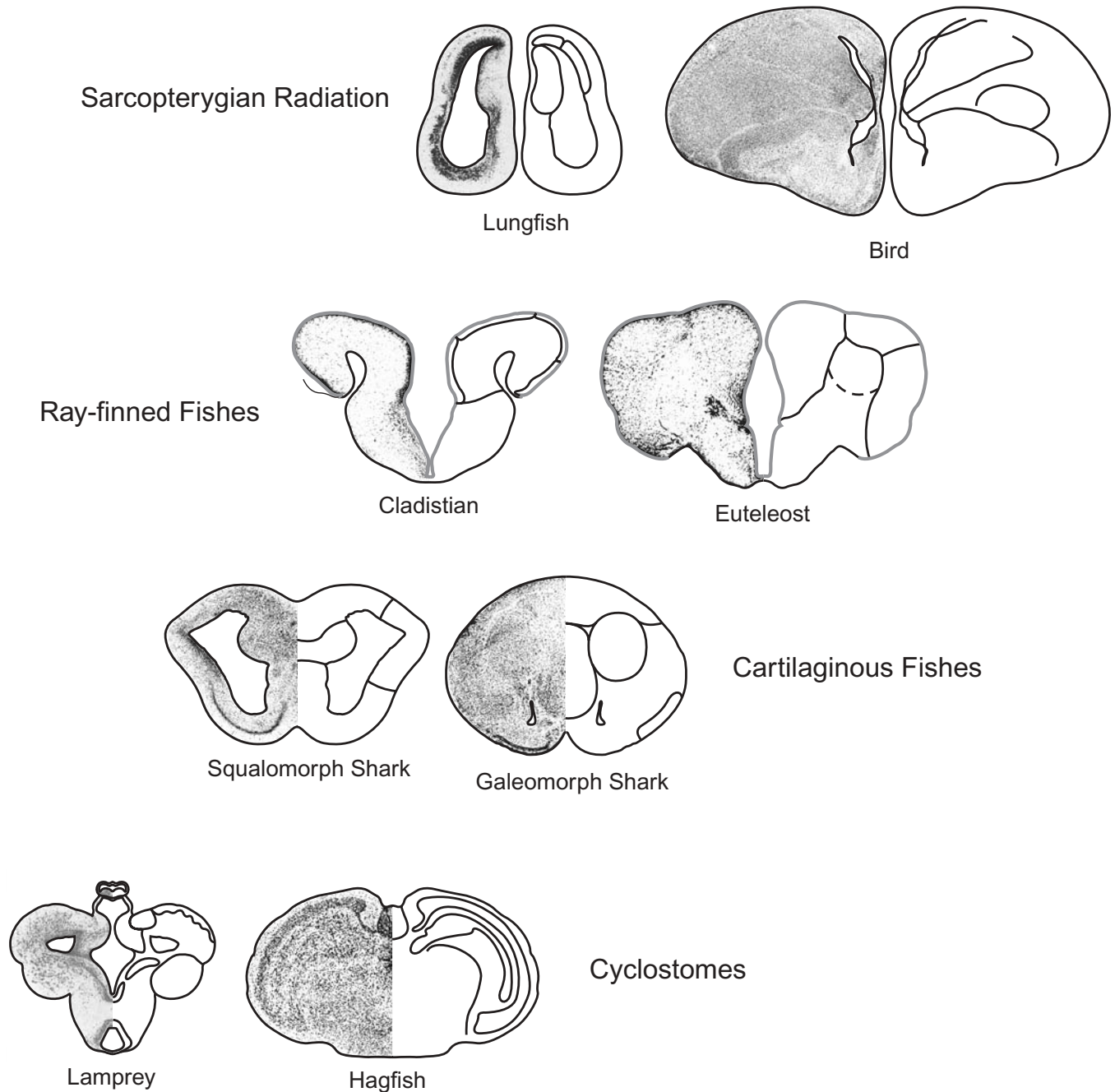


FIGURE 31-11. Nissl-stained hemisections with mirror-image drawings through the telencephalons of a variety of vertebrates to contrast the Type I (lamprey, squalomorph shark, cladistian, and lungfish) brains with the Type II (hagfish, galeomorph shark, euteleost, and bird) brains found in each of the four major vertebrate clades—cyclostomes, cartilaginous fishes, ray-finned fishes, and the sarcopterygian radiation. Sources for figures are as described in other chapters in this book.

hindbrain region would probably have projected rostrally to the roof of the midbrain. Since the roof of the midbrain is devoted to a spatially organized analysis of sensory information in all extant vertebrates, it is highly probable that such a spatial map was present in the midbrain roof in the early, definitive vertebrates. The combination of spatial input from the paired

lateral eyes and from the lateral line and octaval systems in the midbrain roof contributes to the localization of predators and prey, and analysis of this information in the tectum would have provided the basis for its profitable use by the animal.

Little information is available on the early evolution of motor systems and the descending pathways that form them.

A striatal region of the telencephalon and both the roof and tegmentum of the midbrain may have constituted some of the earliest motor-related parts of the brain rostral to the actual motor nuclei of cranial and spinal nerves.

In summary, olfactory (and/or terminal), paired retinal photoreceptive, and pineal-parapineal photoreceptive senses were probably the earliest senses established in the common ancestor of cephalochordates and vertebrates, as were the major subdivisions of the brain: a forebrain with a dien-cephalon, a transitional area that later elaborated into the definitive midbrain, a hindbrain, and a spinal cord. In definitive vertebrates, electroreceptive and mechanoreceptive lateral line, taste, auditory, vestibular, trigeminal, and profundal sensory inputs were established, although not all were evolved simultaneously. Some of the major ascending sensory pathways and descending motor pathways were established. Ascending serotonergic projections from the raphe and descending projections to the spinal cord from the reticular formation and possibly also from vestibular, trigeminal, and solitary nuclei are among the pathways that characterized the brainstem in early vertebrates.

THE ADVENT OF JAWS

The evolution of jaws that could be used for the capture and initial processing of prey into the digestive system was of seminal significance in vertebrate history. Current ideas on how jaws evolved all involve the recruitment of the most rostral of the branchial bars, the mandibular arch, but differences remain to be resolved on how the scenario unfolded. One theory is that of Jon Mallatt, which posits that the initial enlargement of the mandibular arch allowed improved efficiency in ventilation, with subsequent enlargement allowing for suction and grasping prey—a different perspective than the more traditional view involving immediate adaptive advantages for prey capture with the initial phase of mandibular arch enlargement. Along with the changes to the mandibular arch and its associated structures, the forebrain, midbrain, and hindbrain in gnathostomes are all characterized by further developments and specializations related directly or indirectly to the advantages gained by the much more mobile and actively predatory lifestyle. We will survey a number of the features of the brain that evolved within the various radiations of gnathostomes and then consider the various mechanisms that underlie their evolution.

With increased mobility for both prey seeking and predator avoidance, changes that enhanced control of the motor system were strongly selected for. Such enhanced control was partly achieved through the development of the cerebellum in the roof, or rhombic lip, of the hindbrain. Early vertebrates had either only a small cerebellum or no cerebellum at all, with the rhombic lip poorly developed. This part of the brain may have consisted only of an *eminencia granularis*, a cell population associated with the cerebellum itself in gnathostomes, or of an *eminencia granularis* and a small cerebellum. A marked increase of cell proliferation in the rhombic lip occurs during development in gnathostomes and results in the formation of the cerebellum.

The midbrain in early vertebrates would already have been developed to the extent of relaying lateral line, octaval, and

visual information to the forebrain. It would have been organized as a topographic map of external space and would also have played a role in the organization of oriented motor responses to the sensory stimuli. The midbrain roof did not undergo marked changes in organization with the development of jaws, but within different radiations of gnathostomes, this part of the brain was expanded markedly in size and was elaborated in terms of its cytoarchitectonic organization. Its usefulness for spatial analysis and orientation to stimuli continued to be selected for and thereby augmented in various groups.

Within ray-finned and cartilaginous fishes, the dien-cephalon is characterized more by development of the pre-tectum and posterior tuberculum than by development of the dorsal thalamus. The opposite condition—greater development of the dorsal thalamus than pretectal and posterior tubercular regions—characterizes amniotes, as we will consider below. The pre-tectum is elaborately developed particularly in some teleost fishes, in which a variety of pathways relay visual information through a varying series of pretectal nuclei to various sites in the brainstem. One pretectal pathway relays visual information to the inferior lobe of the hypothalamus, which participates in the motor control of feeding behavior.

In both cartilaginous and ray-finned fishes, the posterior tuberculum gives rise during development to a number of laterally migrated nuclei (the preglomerular nuclear complex of ray-finned fishes) that relay ascending lateral line and gustatory information to the forebrain, particularly to the (topologically) lateral pallium—the probable homologue of the frontotemporal amygdala of mammals. The dorsal thalamus in these groups relays some sensory information to the telencephalon but is more simply organized, consisting of only three periventricular nuclei.

Although the dorsal thalamus is not markedly elaborated in cartilaginous and bony fishes, the telencephalon is greatly expanded in some groups within both of these radiations. The telencephalon is also large and complex in hagfishes. Within amniotes, both the dorsal thalamus and the telencephalon are expanded and complex in mammals, in some reptiles, and in birds. These increases in the size of the forebrain have occurred independently. Within each of these various groups of vertebrates, the increase in the size and complexity of the forebrain may be related to actively predacious lifestyles in some cases but may also be correlated with such functions as more complex analysis of sensory information, learning and memory, and social, conspecific interactive behaviors.

The dorsal thalamus of fishes is not elaborated, consisting only of two parts: the *lemnithalamus* predominantly in receipt of lemniscal sensory inputs and the *collothalamus* predominantly in receipt of sensory inputs relayed through the roof of the midbrain. The *lemnithalamus* projects to the (topological) medial pallium and to what has been identified as the dorsal pallium, while the *collothalamus* projects to the striatum. In some cartilaginous and ray-finned fishes, projections of both divisions of the dorsal thalamus also terminate in a pallial region that lies between the (topological) medial and lateral pallia. In sharks, this region is composed of at least two major parts, a dorsal laminar zone and a more ventrally lying zone called the central nucleus. Similarly located regions are present in the telencephalon of many teleosts, particularly in some of the euteleosts in which the telencephalon is strikingly enlarged

and elaborated. Whether these dorsally lying pallial areas in cartilaginous and ray-finned fishes are homologous to the non-limbic pallium of amniotes is an unresolved question, however. Immunohistochemical studies in particular suggest that, more probably, they evolved independently along with the independent expansion of the telencephalon.

ONTO THE LAND AND INTO THE AIR

The conquests of the terrestrial environment and subsequently of the air itself were, like the acquisition of jaws, momentous events in vertebrate history. These new environments presented a multitude of new selective pressures that operated on variations in sensory input systems, information processing areas, and motor control systems in the central nervous system and on their peripheral musculoskeletal counterparts.

In all tetrapods, a dorsal pallial region is present between the medial and lateral pallia, although the evolutionary relationship between the dorsal and lateral pallial areas in amphibians and what is recognized as the dorsal pallium in amniotes is unclear. Also, a more recent recognized ventral pallium lies ventral to the lateral pallium. In ancestral amniotes, two major changes occurred in the development of both the dorsal thalamus and the greater part of the pallium that were strongly selected for. The dorsal thalamus underwent a dual elaboration; that is, in both the lemnothalamus and collothalamus, regionally specific cell proliferation was increased during development in correlation with the lateral (centrifugal) migration of neuron cell bodies. This change resulted in the presence of multiple, migrated nuclei within both parts of the dorsal thalamus. In ancestral amniotes, projections from the lemnothalamus to the medial pallium and to part of the dorsal pallium, the lemnopallium, were present. Projections from the collothalamus to the striatum were also present. In addition, projections from the collothalamus to parts of the dorsal, lateral, and ventral pallia—the collopallium—were acquired. Furthermore, ascending somatosensory projections via the dorsal column nuclei to the dorsal thalamus, both directly and relayed through the roof of the midbrain, also were either acquired or greatly enhanced at this time.

In correlation with the dual elaboration of the dorsal thalamus, a dual expansion of the pallium occurred. Initially in the synapsid line that led to extant mammals, the lemnothalamus and lemnopallium preferentially elaborated, while in ancestral diapsids, the collothalamus and collopallium did so. Subsequently, the collothalamus and collopallium secondarily elaborated in mammals, while the lemnothalamus and lemnopallium secondarily elaborated in the diapsid line, particularly in birds.

Within much of the pallium of early synapsids, developmental changes, including an increase in the radial organization of the neurons and a marked increase in the number of reelin-expressing Cajal-Retzius cells (see Chapter 3), resulted in a novel “inside-out sequence” in the centrifugal migration of neurons, with the consequent formation of the six layers present in neocortex—alike in both its lemnopallial and collopallial components. Increases in cell proliferation also resulted in the presence of new cell types as defined by their immunohistochemical profiles, particularly in layers II–IV of

the neocortex. Subsequently in various separate lineages of mammals, other mutational events produced repeated duplications of various sensory cortical areas, resulting in multiple sensory representations, particularly within the collopallium.

Further mutational events in mammals resulted in a number of new organizational features and structures. The medial pallium was further expanded. A number of ascending connections from the dorsal thalamus were lost, particularly most of those from the contralateral part of the lemnothalamus. Long descending projections from the neocortex and interhemispheric connections via the corpus callosum were gained.

In the diapsid line, marked increases in the area of the collopallium occurred, with the consequent formation of the anterior dorsal ventricular ridge. Expansion of the lemnopallium was relatively minor initially and has remained so in reptiles. Developmental changes to produce increased lamination, such as an increase in radial organization of the proliferated neurons, did not occur in either the lemnopallium or the collopallium, and thus the dorsal ventricular ridge is predominantly characterized by a single cell lamina or by nuclear groups rather than by multiple cortical laminae.

In the ancestral diapsid stock that gave rise to birds, an independent expansion of the lemnopallium occurred, resulting in the formation of the Wulst. Cells with immunohistochemical phenotypes similar to some of those found in layers II–IV of mammalian neocortex were also independently evolved in the dorsal pallium. Regional increases in cell proliferation during embryological development that resulted in an enlarged medial pallium were selected for in birds as well; this phenomenon is particularly evident in birds that sequester stores of food for the winter to which they must repeatedly return to stock and to feed from.

The dual elaboration of both parts of the dorsal thalamus and the dual expansion of the lemnopallium and the collopallium that occurred in ancestral amniotes were strongly selected for. The massive increase in the amount of sensory information reaching the pallium was of great advantage for survival in a terrestrial environment. In correlation with the increased analysis of sensory information, the value of learning and memory is reflected in the further development of the medial pallium, particularly in mammals and likewise to some extent in birds.

In ancestral amniotes, a new set of selective pressures also affected the evolution of somatosensory and motor control systems for survival in the terrestrial environment. These systems have been elaborated to some extent independently in the synapsid line and in birds. In mammals, sensorimotor cortex, a part of the lemnopallium, is well developed and distinct from other cortical areas. Similarly, in birds, the somatosensory part of the Wulst is well developed and, like motor cortex in mammals, gives rise to a long, descending, pyramidal motor tract. Additionally in birds, a more caudal, superficially lying region in the telencephalon may play a major role in motor control via influences on the striatum.

Motor control pathways vary among amniotes as a consequence of differential selective pressures. In both mammals and birds, selective pressures have favored motor control mediated by pathway loops through the striatopallidum and dorsal thalamus to the sensorimotor cortex and back to the striatopallidum, similar loops involving the cerebellum, and by

long descending pathways to the brainstem and spinal cord from sensorimotor cortex. These loops and associated complex motor pathways also support high levels of vocal control in songbirds and parrots. Pathways from the striatum to the optic tectum via the pretectum and substantia nigra are relatively minor, particularly in mammals. In reptiles, selective pressures have favored striatal pathways to the optic tectum via the pretectum and/or the substantia nigra, with less elaboration of the striatopallidal and cerebellar loop systems and with the apparent absence of a pyramidal tract.

THEORIES OF VERTEBRATE BRAIN EVOLUTION

The invasion hypothesis of vertebrate brain evolution dominated the first half of the twentieth century. This hypothesis held that changes in central nervous system connections occur as a result of axon collaterals invading and forming new connections with a given group of neurons. In particular, the telencephalon was thought to have been dominated ancestrally by olfactory input and that other sensory systems later invaded the telencephalon and competed with olfactory fibers for synaptic sites, eventually establishing their own areas of pallial territory. This hypothesis may well contain at least some correct elements but for the wrong reasons. It was based on the belief that the brains of most extant anamniote vertebrates are predominantly in receipt of olfactory input and do not have the ascending sensory inputs from the nonolfactory senses that amniotes do. While olfaction was one of the earliest senses to evolve in vertebrates, the rest of the major sensory pathways to the telencephalon were also established relatively early in vertebrate history.

A more recently proposed hypothesis, Sven Ebbesson's parcellation hypothesis, is in some respects the mirror image of the invasion hypothesis. The parcellation hypothesis holds that the brain has changed over evolution by the selective loss of connections and the concomitant segregation of neuronal populations. As opposed to new neuronal groups and connections being added in the brain over time, the parcellation hypothesis suggests that a more diffusely organized amalgam of neurons and connections goes through a process of attrition and sorting out over time, resulting in the discrete nuclei and connections present in extant vertebrate brains.

The equivalent cell hypothesis of Harvey Karten created a revolution in comparative neuroanatomy in the 1960s. This hypothesis derived from studies of ascending sensory pathways in birds and focused on the evolution of the telencephalon in amniotes. Crucially, it established unequivocally that large areas of the telencephalon were pallial rather than subpallial (striatopallidal). It argued that various cell populations that form nuclear groups within the dorsal ventricular ridge in birds and reptiles are comparable to groups of neurons within specific layers of mammalian neocortex that have similar respective connections. Furthermore, these cell populations in diapsids and their respective comparable cell populations within neocortex in mammals were inherited from the common ancestral stock of amniotes and are thus respective homologous cell populations.

The problem of whether part of the dorsal pallium of ancestral amniotes developed into a dorsal ventricular ridge or had an neocortical structure or neither has been the subject of continuing debate. Glenn Northcutt argued that expansion of the dorsal pallium occurred independently in synapsids and diapsids and that parts of mammalian neocortex and the dorsal ventricular ridge are thus homoplastic. More recent molecular studies by Luis Puelles, John Rubenstein, and their co-workers and colleagues have shown similarities in gene expression patterns that are shared by the diapsid dorsal ventricular ridge and the lateral and ventral pallia, rather than the dorsal pallium, of mammals. These studies have challenged parts of Karten's equivalent cell hypothesis. Part of the resolution to this persistent mystery may lie in looking for field homologies, such as a possible one of the anterior dorsal ventricular ridge to all parts of the collopallium of mammals, including the laterally lying parts of neocortex and the collothalamo-recipient and related parts of the amygdala. Another key to the resolution may lie in gaining a better understanding of the amygdala itself, appreciating its various divisions as elaborations of the deep layers of the cortical mantle and of the underlying striatum, as proposed by Larry Swanson and Gorica Petrovich. Whatever the resolution and the specific or field homologies of the collopallium across amniotes, the striking differences in cytoarchitecture combined with the remarkable similarities of function between birds and mammals in terms of complex cognitive abilities presents an even more intriguing enigma.

HOW VERTEBRATE BRAINS EVOLVE

In this book, many differently evolved parts of the brain in diverse groups of vertebrates have been discussed. We can now generate at least a partial list of the variety of ways in which vertebrate brains evolve.

Induction is one of the most basic mechanisms involved in the evolution of the vertebrate central nervous system. The most salient example of this phenomenon is the origin of the vertebrate central nervous system from the nerve net-like condition of the earliest deuterostome ancestral stock. The localized development of ectodermal neural tissue along the dorsal sector of the rostrocaudal axis in vertebrates (and the homologous ventral sector in most invertebrates) occurs as a result of chordin/sog (short gastrulation) produced by the mesoderm and the consequent blockage of BMP (bone morphogenetic protein)/dpp (decapentaplegic) receptor sites, allowing a neural fate for the ectoderm in the affected region. At the origin of vertebrates, the enlargement and elaboration of the central nervous system, including paired lateral eyes, were subsequently capitalized on by the elaboration of neural crest and the formation of neurogenic placodes, with the peripheral nervous system complement of sensory system structures and other neural crest derivatives thereby produced.

A second basic mechanism of vertebrate brain evolution, and likewise of brain elaboration in arthropods and cephalopod molluscs, involves the rostrocaudal specification of regions within the brain. How homeobox genes, present in the ancestral bilaterian stock, shifted or extended their functional influence to specify a detailed neuromeric organization within the various elaborated central nervous systems is one of the most

important remaining questions in brain evolution. Within the vertebrate lineage, the neuromeric patterning established in the earliest vertebrates has been preserved in all descendant groups.

The high degree of similarity in the genetic mechanisms for induction and patterning of the nervous system across the diverse taxa that exhibit enlarged, elaborated central nervous systems—arthropods, cephalopod molluscs, and vertebrates—indicates that the potential for this elaboration already was established in the earliest urbilaterian ancestral stock of the radiation of all bilaterally symmetrical animals. The same sets of patterning genes have been inherited in the different lineages. Since brain elaboration did not characterize the urbilaterian ancestor and has not occurred in many of the descendant invertebrate taxa, the brains of arthropods, cephalopod molluscs, and vertebrates are not homologous in the historical sense. Nonetheless, their sameness in terms of both genetic and structural correspondences is clearly apparent. They do fall within the more encompassing rubric of generative homology, or syngeny, as the same products of homologous genes, with the genes themselves inherited from a common ancestor.

Focusing now on the vertebrate lineage, a number of additional mechanisms for nervous system evolution can be noted, some of which overlap and/or complement each other. Invasion has occurred in various instances. In the earliest definitive vertebrates, some of the new sensory systems that were developed as a result of the evolution of neural crest and placodes projected into the hindbrain and were relayed via the midbrain and diencephalon to the newly acquired telencephalon. These new incoming, ascending projections and the synaptic territories that they established are perhaps the ultimate example of invasion. The evolutionary development in ancestral amniotes of new projections from the collothalamus to the pallium in addition to the existing projections to the striatum is a second example of invasion, and evidence suggests that this invasion occurred as a result of collateralization, which is one of the originally hypothesized mechanisms for invasion.

Parcellation has occurred in some instances. One of the best examples of this process may be in some of the changes associated with the elaboration of the lemnothalamus in ancestral amniotes. The single nucleus, nucleus anterior, present in anamniotes appears to be homologous as a field to multiple nuclei in the dorsal thalamus in amniotes. These multiple nuclei each do not have all of the afferent and efferent connections that the nucleus anterior has in anamniotes. The embryological development of the lemnothalamus in amniotes is such that connections and cell groups are segregated relative to the condition in anamniotes.

Loss of connections *per se*, that is, in the absence of the parcellated segregation of cell groups, has also occurred. The lemnothalamus gives rise to bilateral projections to the pallium in anamniotes. In amniotes, some of the projections to the contralateral side are maintained, but some have been lost. This loss has been most extensive in mammals.

Developmental differentiation of a specific embryonic field into multiple nuclei instead of just one nucleus has occurred in some instances. The evolution of the lemnothalamus in amniotes mentioned above is one example of this phenomenon. A second example occurs in the pretectum of percomorph euteleosts, where two nuclei, nuclei pretectalis

superficialis pars intermedius and glomerulosus, are present instead of the single nucleus, nucleus posterior, which is present in most other groups of ray-finned fishes. Other examples of this phenomenon are the presence of new, unique nuclei within particular species or groups, such as the electromotor control systems of some electric fishes and the elaborate, descending motor pathways for vocal control in songbirds and parrots.

Duplication of neural regions has occurred in a number of instances, particularly in the evolution of collopallial neocortical sensory areas in various groups of mammals. Mutational events have occurred that have resulted in the production during development of multiple “copies” of the substantially fewer areas present in ancestral synapsids. Similar duplications may have occurred independently in birds, particularly in the auditory collopallium.

The most frequent mechanism of central nervous system evolution may be regionally specific changes in neuron proliferation. Whereas the specification of dorsoventral and rostrocaudal parts of the brain is regulated by homeobox gene function, differences in local neural proliferation may be under the control of other mutational events. Regional increases in proliferation usually occur in association with one of several related developmental phenomena.

The continuation of proliferation paired with centrifugal migration of neurons away from the periventricular matrix accounts for the evolution of both the lemnothalamus and the collothalamus in amniotes and of the enlargement of the dorsal ventricular ridge in some reptiles and in birds. The evolutionary elaboration of the cerebellum in jawed vertebrates as well as in some fishes, such as mormyrids, is a third example of this process.

The continuation of proliferation paired with migration of neurons in the presence of increased radial organization and a marked increase in the number of reelin-expressing Cajal-Retzius cells accounts for the change from an “outside-in” developmental sequence to the “inside-out” developmental sequence that produces the six neocortical layers present in most of the mammalian pallium. In contrast, nuclear groups result from “outside-in” neuronal migration, as is the case in the dorsal thalamus of all amniotes and in the dorsal ventricular ridge of sauropsids.

The continuation of proliferation paired with differentiation, as a result of mutational events, of the migrated neurons accounts for the presence of new phenotypes of neurons. An example of this phenomenon is the presence of neurons in some layers of mammalian neocortex that have neurotransmitter- and neuropeptide-specific profiles not found in the pallium of most nonsynapsid amniotes. Some neurons with mammalian-like phenotypes are present in birds, having been independently evolved as the result of similar mutational events.

Thus, evolution of the vertebrate central nervous system has occurred by the following phenomena:

- induction;
- homeobox gene patterning;
- invasion;
- parcellation;
- loss of connections *per se*;

- developmental differentiation of multiple nuclei;
- duplication of neural areas;
- regionally specific changes in neuron proliferation paired with lateral or centrifugal migration, changes in the degree of radial organization, and/or differentiation of new neuronal phenotypes.

These phenomena all can be influenced by relatively simple mutational events that thus can become established in a population as the result of random variation. Selective pressures acting on a given population then determine whether the phenotypes produced by these random mutations increase their proportional representation within the population and eventually become established as the normal condition. The functional correlates of the phenotypic expressions of central nervous system organization are the abilities for sensory processing; information storage, retrieval, and analysis; and motor response repertoires of the animal. The adaptive advantages conferred by an organized nervous system as opposed to a nerve net, by a variety of specific sensory input systems, by the gain of some new connections and the loss of some established connections, by the formation of multiple new nuclei through elaboration or duplication, and by regionally specific increases in cell proliferation in many different parts of the brain have determined the course of brain evolution across the vertebrates and likewise across the invertebrate radiation as well.

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Appendix

Terms Used in Neuroanatomy

INTRODUCTION

Anatomists have devised a set of terms that they find useful in indicating the location of structures, directions, and planes of section. These terms are nearly all in Latin or Greek, or are derived from them. Newcomers to the field often are baffled by these terms and wonder why simple words like “front,” “back,” “top,” and “bottom” cannot be used instead. Part of the answer is that the specialized anatomical terms often provide greater precision. Moreover, the use of these terms is a centuries-old tradition that originated in the days when the language of science was Latin and when many educated persons also were familiar with classical Greek. Another reason is that anatomy is an international discipline. Anatomists publish the results of their research in many languages. By using an international nomenclature based on Latin and Greek, a number of communication barriers are lowered. This advantage applies not only to the direction and location terms but to the names of brain regions and subdivisions as well as the individual cell groups and fiber pathways that comprise the nervous system.

In this appendix, we will describe and define many of the common terms that anatomists use to indicate relative and absolute direction and the location of structures. In addition, we will present a listing of the Latin and Greek derivations of many of the terms that you will encounter in this book. These include nouns and their modifiers and prefixes. Our hope is that understanding the meanings of some of these structure names will help you to remember them better because you will be able to associate a visual image with the name.

DIRECTION AND LOCATION TERMS

The most elementary of directional terms are those that indicate front and back. These are **anterior** (front) and **posterior** (back) and are illustrated in the drawing in Figure A-1(A). The drawing shows a ray-finned fish with the location of the brain and spinal cord indicated. The front and back ends of an animal can be called **rostral** (the snout end) and **caudal** (the tail end), respectively. In a legless animal, such as a fish or a snake, the terms anterior and rostral may be freely interchanged as can posterior and caudal. Another term that sometimes is encountered is **oral**, which literally means in the direction of the mouth, but which often is used interchangeably with rostral. Two other basic directional terms are shown in Figure A-1(A). These are **dorsal**, meaning in the direction of the back, and **ventral**, meaning in the direction of the abdominal surface.

Figure A-1(B) shows the same terms applied to a tetrapod, that is, a four-legged animal. Again, note the location of the brain and spinal cord. The basic directional terms apply just as well to a tetrapod as to a legless animal. Some confusion occurs, however, when we attempt to transfer this simple system of terms to bipeds, that is, two-legged animals. To understand the logic of the transfer, the reader should study Figure A-2, which shows a typical biped in a rather atypical posture. When a human is seen assuming the tetrapod posture, the basic directional terms apply rather well. This, however, is not the normal human posture. When humans are viewed in their normal, upright posture, strange things happen to their directional terms as can be seen in Figure A-3, which shows an upright human and another upright biped.

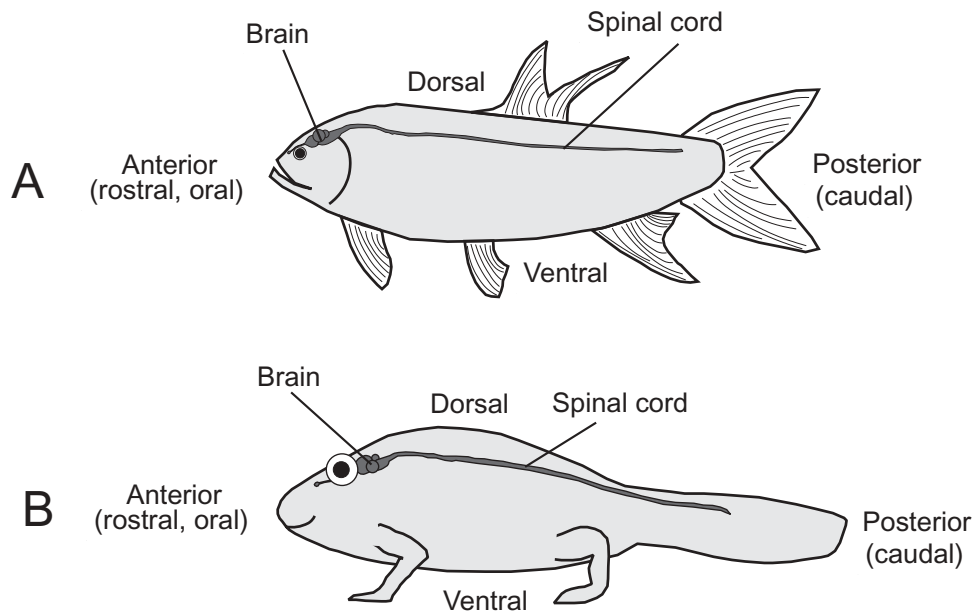


FIGURE A-1. Basic anatomical directional terms are illustrated in a drawing of a ray-finned fish (A) and a tetrapod salamander (B). The location of the brain and spinal cord are shown.

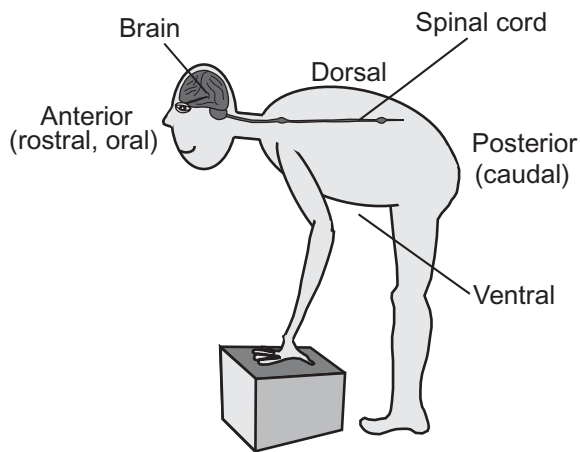


FIGURE A-2. Basic anatomical directional terms are illustrated in this drawing of a biped human who is assuming a tetrapod position. The location of the brain and spinal cord are shown.

When a biped is in the upright position, dorsal and posterior become the same, as do ventral and anterior. Rostral still refers to the snout or head end, but that is no longer anterior. In contrast, caudal is still posterior. Notice also that the spinal cord is at right angles to the brain in the bipeds, whereas it lies on an axis parallel to that of the brain in the tetrapod and legless animals. Thus, in a biped, the dorsal surface of the spinal cord is also the posterior surface.

Figure A-4 introduces several additional directional terms. **Lateral** means the side of the body, and **medial** means the midline of the body. In addition, **unilateral** means one side, **bilateral** means two sides or both sides, **contralateral** means

the opposite side, and **ipsilateral** means the same side. The relative positions above and below are indicated by the terms **superior** and **inferior**, respectively. The terms superior and inferior have nothing to do with the quality or degree of complexity of the structures to which they are applied. They indicate relative position and nothing more. Other relative terms are **proximal**, meaning near, **distal**, meaning far, **para-**, meaning adjacent to, and **sub-**, meaning below.

PLANES OF SECTION

Anatomists nearly always cut their specimens into thin slices called sections, which they examine with the light microscope or electron microscope in order to observe the fine details of their structure. Because a group of cells may have a very different shape when viewed from a different direction, anatomists always indicate the plane in which the specimen has been cut. Figure A-5 is a schematic representation of the most common planes of section. The planes are represented on a cylinder.

The two major planes of section are the **transverse** and the **longitudinal** planes. The most frequently used plane of section is the transverse plane. Sections cut in this plane are sometimes called **coronal** or **frontal** sections. Transverse sections are cut *across* the long axis of the cylinder; that is, parallel to the diameter of the cylinder. Longitudinal sections are cut *along* the long axis of the cylinder. The longitudinal plane that is vertically oriented and divides the cylinder into two symmetrical halves is known as the **midsagittal** plane. Sections that are cut parallel to the midsagittal plane are properly called **parasagittal** sections. In common usage, however, they usually are simply called **sagittal** sections. Sections that are cut parallel to the long axis of the cylinder and also at right angles

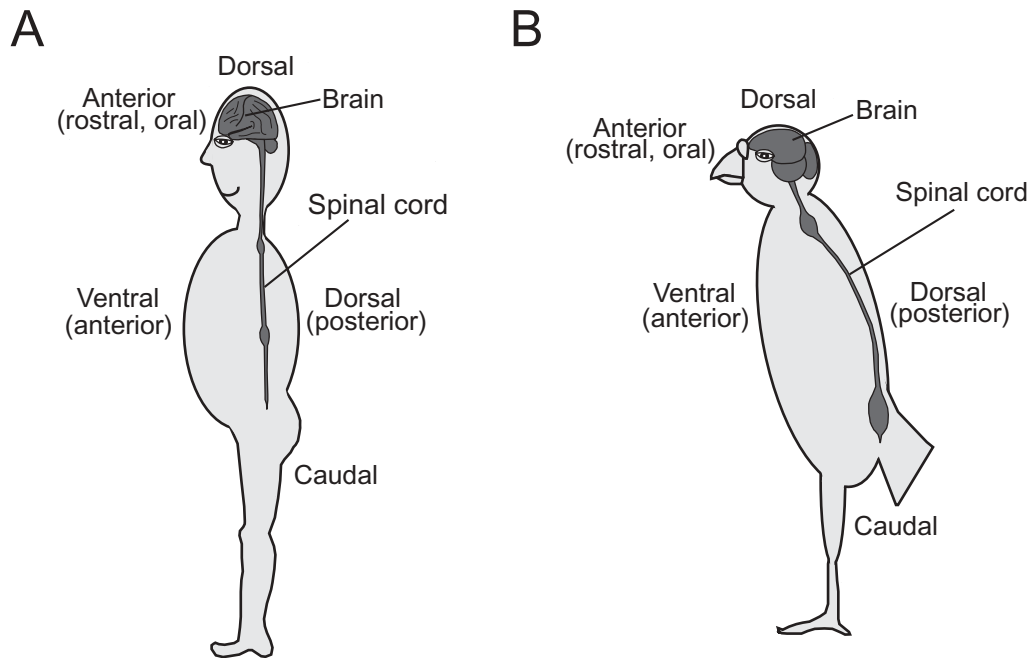


FIGURE A-3. Basic anatomical directional terms are illustrated in this drawing of two bipeds, a human (A) and a bird (B). Both animals are standing in their normal, biped posture. The locations of their brains and spinal cords are shown. Note how the terms *anterior* and *posterior* now correspond to *dorsal* and *ventral* as a consequence of the upright posture.

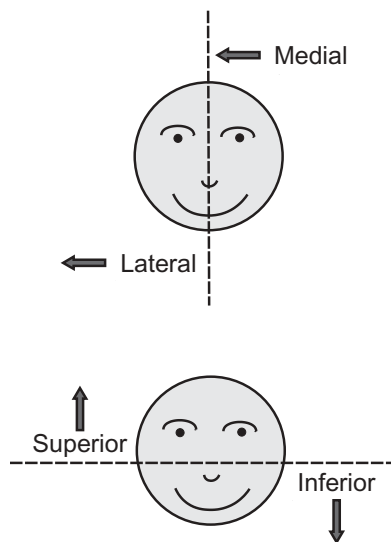


FIGURE A-4. Additional directional terms; *medial*, meaning toward the midline, *lateral*, meaning toward the side, *superior*, meaning above some reference point, and *inferior*, meaning below some reference point.

to the midsagittal plane are known as **horizontal** sections. Both the sagittal and horizontal planes are the conventional planes for longitudinal sections.

Occasionally, an anatomist may have need to cut sections in a plane other than one that is parallel or at right angles to the main axes of the cylinder. Such a plane is known as an

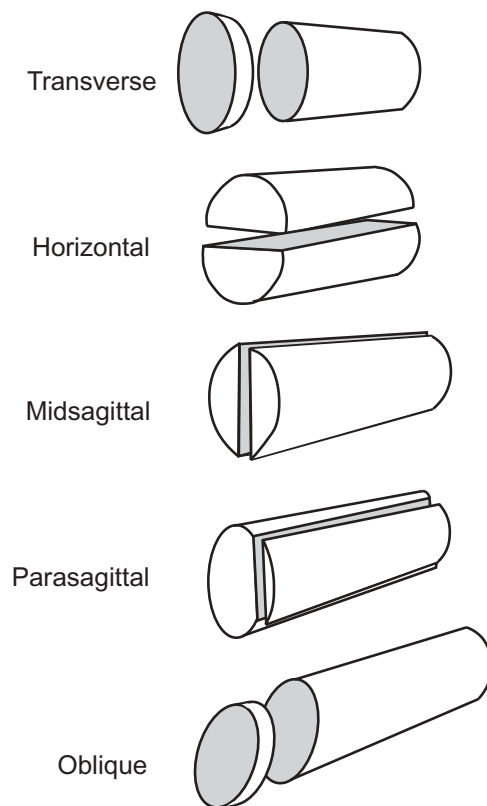


FIGURE A-5. The most common planes of section of neural tissue are illustrated as slices through a cylinder.

oblique plane. Sometimes anatomists deliberately use an oblique plane of section to reveal certain relationships between two or more structures that otherwise would not appear in the same section. Oblique planes of section also result unintentionally when, for some reason, the long axis of the brain or spinal cord is not aligned at an exact right angle to the plane of the blade of the cutting device. One of the infinite number of oblique planes is illustrated in Figure A-5.

NEUROANATOMICAL NAMES

Nearly all of the names given to anatomical entities, whether cell groups or gross structures, are Latin or Greek names. Not very long ago, when knowledge of Latin and Greek was common among educated persons, the terms given below would have posed no serious challenge. Today, however, when the study of these languages is a relative rarity, the terms often seem to be a hindrance to learning rather than a help. A list of neuroanatomical term derivations is presented below. It gives the root and its language (G for Greek or L for Latin), the English translation, and a neuroanatomical example. Please note that many of the terms specified below as being of Latin derivation have equivalent Greek terms, since the Romans borrowed many of their terms from the Greek language. The purpose of this list is to help you to understand the meanings of many of the neuroanatomical terms that you will encounter in this book and in the scientific literature.

DERIVATION OF TERMS

Root	Origin	Translation	Example
a-, an-	G	not, without	anencephalic
abduco	L	to abduct, take away	abducens nerve
akouein	G	to hear	statoacoustic nerve
ala	L	wing	alar plate
alba	L	white	stratum album centrale
allos	G	other	allocortex
alveus	L	trough or canal	alveus hippocampi
ammonis	L	of Ammon, from the Egyptian god Amun Kneph	cornu ammonis
amygdale	G	almond	amygdala
ansa	L	handle of a jug	ansa lenticularis
ante-, anterior	L	before, toward the front	nucleus anterior
arachnes	G	spider	arachnoid mater
arbor	L	tree	arbor vitae
arch-, archi-	G	beginning, old	archicortex
arco-	L	arched	arcopallium antierius
arcuatus	L	curved, as a bow	internal arcuate fibers
astron	G	star	astrocyte
axon	G	axis	axon
basis	L	base, step, foundation	basis pedunculi
brachium	L	arm	brachium pontis
bulbus	L	onion	corticobulbar tract
calcar	L	spur, bird's claw	calcarine fissure
callosus	L	hard	corpus callosum
capere	L	to take	exteroception
cauda	L	tail	caudate nucleus
cerebellum	L	little brain	corpus cerebelli
cerebrum	L	brain	cerebral cortex
chi, chiasm	G	the letter chi, two crossing lines	optic chiasm
chorion	G	delicate membrane	choroid plexus
cilium	L	eyelash	ciliary ganglion
cinereus	L	ashen	tuber cinereum
cingulum	L	girdle, belt	cingulate gyrus
claustrum	L	an enclosed space or barrier	claustrum
cochlea	L	snail or shell	cochlea
coeruleus	L	sky blue	locus coeruleus
colliculus	L	mound, little hill	superior colliculus
com-	L	together	posterior commissure
conjungere	L	to join together	brachium conjunctivum
cornu	L	horn	cornu Ammonis
corona	L	crown	corona radiata
corpus	L	body	corpus Luysii
cortex	L	bark	neocortex
crista	L	crest	crista cerebellaris
crus	L	leg	crus cerebri
cuneus	L	wedge	cuneus
declivis	L	sloping	declive
decussare	L	to intersect, from the Roman numeral X (decem)	decussation of Meynert
dendron	G	tree	dendrite
dentatus	L	toothed	dentate gyrus
derma	G	skin	endoderm
dia-, di-	G	through	diencephalon
dorsum	L	back	dorsal longitudinal fasciculus
dromos	G	running	orthodromic
dura	L	hard or strong	dura mater
effere	L	to carry out from, from	efferent
ektos	G	outside	ectoderm
en-, ent-, ento-	G	in, inside	entopallium
endyma	G	garment	ependyma
enkephalos	G	brain	telencephalon
epi-	G	upon	epithalamus
equus	L	horse	cauda equina

Root	Origin	Translation	Example	Root	Origin	Translation	Example
externus	L	outside	nucleus cuneatus externus	inter-	L	between	interpeduncular nucleus
facies	L	face, countenance	facial nerve	intercalare	L	to insert	hyperpallium intercalatum
falx	L	sickle	falx cerebri	internus	L	internal	internal capsule
fascia	L	ribbon or band	fascia dentate	iso-	G	equal	isocortex
fascis	L	bundle	fasciculus cuneatus	isthmus	G	narrow part connecting two larger parts, neck	nucleus isthmi
ferre	L	to carry	efferent	juxta-	L	near to, close by	juxtarestiform body
filum	L	thread	filum terminale	kampos	G	sea monster, caterpillar	hippocampus
fimbria	L	fringe	fimbria hippocampi	kephale	G	head	mesencephalon
fissura	L	cleft or slit	lateral fissure	konarion	G	small cone	conarium (=pineal gland)
flectere	L	to bend	fasciculus retroflexus	konis	G	dust	koniocortex
flocculus	L	little tuft of wool	flocculonodular lobe	lagena	L	flask	lagena
folium	L	leaf	folia cerebelli	lamina	L	plate or layer	lamina terminalis
foramen	L	opening, from to bore	interventricular foramen	lemma	G	husk	neurolemma
forceps	L	a pair of tongs	forceps minor	lemniskos	G	band or ribbon	medial lemniscus
forma	L	form	restiform body	lens	L	lentil	lentiform nucleus
fornix	L	arch	fornix	leptos	G	delicate	leptomeninx
fossa	L	ditch	interpeduncular fossa	limen	L	threshold	limen insulae
fovea	L	pit	fovea centralis	lingua	L	tongue	lingual gyrus
frenulum	L	small bridle	frenulum veli medullaris rostralis	lissos	G	smooth	lissencephaly
funiculus	L	small cord	dorsolateral funiculus	locus	L	place	locus coeruleus
fusus	L	spindle	intrafusal muscle fibers	luteus	L	saffron-yellow	macula lutea
ganglion	G	swelling	ganglion impar	macros	G	large	macroglia
geniculum	L	small knee	dorsal lateral geniculate nucleus	macula	L	spot	macula lutea
genu	L	knee	genu of corpus callosum	magnus	L	large	nucleus raphe magnus
glia	G	glue	oligodendroglia	mamilla	L	little breast	mammillary body
globus	L	ball or globe	globus pallidus	mater	L	mother	pia mater
glomerulus	L	little ball	olfactory glomerulus	medulla	L	marrow	medulla oblongata
glossa	G	tongue	hypoglossal nerve	meninx	G	membrane	leptomeninx
gracilis	L	slender	nucleus gracilis	meros	G	part	prosomere
gyrus	L	circle	cingulate gyrus	mesos	G	middle	mesencephalon
habenula	L	bridle, rein, or strap	habenula	met-, meta-	G	after, behind	metencephalon
helix	G	coil	helicotrema	mittere	L	to put	anterior commissure
hippos	G	horse	hippocampus	myelos	G	marrow	myelencephalon
hyper-	G	beyond, above, excessive	hyperpallium apicale	neo-	G	new	neocortex
hypo-	G	under	hypoglossal nucleus	neuron	G	nerve	neuropil
impar	L	unequal, having no fellow, hence single	ganglion impar	nido-	L	nest	nidopallium
infundibulum	L	funnel	infundibulum	nocere	L	to injure	nociception
insula	L	island	insular cortex	nodulus	L	little knot	nodulus cerebelli
				nodus	L	knot	nodose ganglion
				nuncius	L	messenger	internuncial neuron
				obex	L	barrier	obex
				oblongus	L	oblong	medulla oblongata
				oculus	L	eye	oculomotor nerve
				olfacere	L	to smell	olfactory bulb
				oligos	G	scanty	oligodendroglia
				opticus	L	seen, visible	optic nerve
				pachy-	G	thick	pachymeninx
				pallidus	L	pale	globus pallidus

Root	Origin	Translation	Example	Root	Origin	Translation	Example
pallium	L	cloak	dorsal pallium	syn-	G	together, same	synencephalon
par-, para-	G	next to, near	paraflocculus	tainia	G	band, tape	tenia (taenia) tecta
parvus	L	small	parvicellular	tapetum	L	carpet or tapestry	tapetum of corpus callosum
peduncle	L	little foot	cerebral peduncle	tectum	L	roof	optic tectum
peri-	G	around	perirhinal cortex	tegmen	L	cover	midbrain tegmentum
pes	L	foot	pes hippocampi	telos	G	end	telencephalon
petra	G	rock	inferior petrosal ganglion	thalamus	G	inner chamber, bedroom	dorsal thalamus
pharugx	G	throat	glossopharyngeal nerve	theca	G	case, sheath	theca lenticularis
pilos	G	felt	neuropil	torus	L	swelling	torus semicircularis
pineus	L	relating to pine, shaped like a pine cone	pineal body	trema	G	hole	helicotrema
piriform	L	pear-shaped	piriform cortex	trigeminus	L	threefold, triple	trigeminal nerve
plexus	L	something woven, a braid	brachial plexus	trochlea	G	pulley	trochlear nerve
pons	L	bridge	brachium pontis	tuber	L	knot, swelling	tuber cinereum
poros	G	passage	neuropore	uncinatus	L	hook-shaped	uncinate fasciculus
principalis	L	first, chief	nucleus opticus principalis thalami	uncus	L	hook	uncus
putamen	L	peel, husk	putamen	uvula	L	little grape	uvula vermis
raphe	G	seam	raphe nuclei	vagus	L	wandering	vagus nerve
restis	L	rope	restiform body	velum	L	veil, covering	velum interpositum
reticulum	L	small net	reticular formation	venter	L	belly	nucleus dorsalis intermedius ventralis anterior
retro-	L	back, behind	fasciculus retroflexus	ventriculus	L	small cavity	lateral ventricle
rhis	G	nose	rhinal sulcus	vestibulum	L	entrance-court, courtyard	vestibular nuclei
rhombos	G	rhomb or lozenge	rhombencephalon	vitae	L	of life	arbor vitae
robustus	L	firm, solid, strong	nucleus robustus arcopallii	<hr/> FOR REFERENCE AND FURTHER READING <hr/>			
rostrum	L	beak	rostrum of corpus callosum				
saeptum	L	wall, partition	septal nuclei	<hr/>			
splenium	L	bandage	splenium of corpus callosum				
stratum	L	layer or blanket	stratum opticum	<hr/>			
stria	L	furrow	stria terminalis				
striatus	L	striped, furrowed	corpus striatum	<hr/>			
subiculum	L	small support	subiculum				
substantia	L	substance	substantia nigra	<hr/>			
sulcus	L	groove or furrow	calcarine sulcus				
supra-	L	above	supraoptic nucleus	<hr/>			

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Glossary

Abducens Sixth cranial nerve (VI); one of three cranial nerves that innervate eye muscles.

Acousticolateralis system See Octavolateralis system.

Actinistia One of the three radiations of sarcopterygians, of which only one species, the coelacanth *Latimeria chalumnae*, is extant.

Actinopterygians The subclass of Osteichthyes, or bony fishes, that comprise the ray-finned fishes.

Adaptation General process by which a species adjusts to environmental change; a feature of an organism that is suited to the environment.

Adaptation studies Studies of similar adaptations in various taxa whether or not the adaptations have been evolved independently.

Advanced Recent, that is, more recently derived from the ancestral stock; can imply progressive “improvement” in a lineage.

Afferent An axon that projects to the central nervous system or to a specific part within it.

Agnatha Jawless fishes, also called cyclostomes. Extant agnathans are the monophyletic group of lampreys and hagfishes.

Allele Alternate form of a gene.

Allometry Study of relative or proportional size, weight, volume, or other such feature among members of a taxon, such as brain weight/body weight ratios.

Ammocoete Larval lamprey.

Amniotes Mammals, reptiles, and birds: animals characterized by the embryo having an amnion, the membrane that surrounds the embryo and the amniotic fluid.

Amphibians Group of tetrapods that generally have aquatic larvae and terrestrial adults; comprise salamanders and newts, frogs, and gymnophionans.

Amphioxus One of the common names for the cephalo-chordate *Branchiostoma sp.* Also known as lancelets.

Ampulla A small, flask-like organ, such as those of the semi-circular canals and electroreceptors.

Anagenesis Used variably to mean (1) progressive evolution or improvement within a lineage toward a “higher” level; see *Scala naturae*; (2) increased efficiency of design of a structure within a lineage; or (3) phenotypic or genotypic changes within a single, unbranched lineage. See also Phyletic evolution.

Analogy Similarity of function. This term is independent of considerations of phyletic continuity.

Anamniotes Include jawless vertebrates, cartilaginous fishes, ray-finned fishes, lungfishes, crossopterygians, and amphibians. An amnion is not present around the embryo during development in these vertebrates.

Anapsids The ancestral amniote stock; the anapsid skull has a complete roof of bone, without fenestrae or arches, in the temporal region.

Anlage Plural: Anlagen. A German term that denotes the primordium of an organ or body part that forms during embryological development.

Anterodorsal lateral line nerve One of three preotic lateral line cranial nerves (LL_{AD}).

Anterograde Proceeding forward; in neuroanatomy, used to mean the direction toward the axon terminal.

Anteroventral lateral line nerve One of three preotic lateral line cranial nerves (LL_{AV}).

Anurans Amphibians without tails in the adult form, the frogs and toads: one of the three extant groups of amphibians.

Apomorphy Adjective: Apomorphic. Traits that are derived specializations of a particular taxon relative to ancestral taxa in which the trait was not present, for example, mammary glands and hair are *apomorphic* for mammals in that they are not present in any other taxon. See also Plesiomorphy.

Arachnoid Middle of three meninges (membranous layers of connective tissue) that cover the brain and spinal cord in

mammals and birds; named for its similarity in appearance to a spider web.

Archenteron Gastrocoel: embryonic gut cavity formed within the gastrula.

Autonomic nervous system Neuronal system that regulates the viscera, such as the smooth muscles of the digestive and circulatory systems, and secretion of glands. Consists of three divisions: the sympathetic division, which has its neurons in the thoracic and lumbar regions of the spinal cord; the parasympathetic division, which has its neurons in the brainstem and sacral region of the spinal cord; and the enteric division, which is a semi-autonomous system that regulates the action of the gut. Although there are exceptions, in general, the sympathetic division upregulates visceral functions and the parasympathetic system downregulates visceral functions. In addition, the three systems work in concert to regulate normal visceral functioning.

Axon The long process of a neuron that carries action potentials to the axon terminal.

Blastocoel Cavity formed within the blastula.

Blastopore Opening of the archenteron.

Blastula Early embryo stage in which the cells form a hollow sphere.

Boutons Also: Boutons terminaux (terminal buttons). French term for axon terminals.

Brainstem Commonly used to refer to the hindbrain, midbrain, and diencephalon; sometimes refers to only the hindbrain (without the cerebellum) and midbrain.

Branchial Refers to the gills, as in branchial arches.

Branchial arches Part of the series of visceral arches that support the gills in fishes. Most fishes have five branchial arches that are the third through the seventh visceral arches. See also Visceral arches.

Branchiomic Refers to the muscles and other structures of the gill arches.

Caecilians See Gymnophionans.

Cenozoic era Geologic time from 65 million years ago to the present, divided into the Tertiary period of 65 to 2 million years ago and the Quaternary period of the past 2 million years.

Central canal Longitudinal, tubular, midline cavity present in the spinal cord; contains cerebrospinal fluid.

Cephalochordates Group of chordate animals that include lancelets of the genus *Branchiostoma*, which is also called by the common name amphioxus.

Cerebellum The dorsal region of the metencephalon, which consists of a cortical sheet or plate, sometimes highly folded, and one or more deep nuclei. Among its many functions in various species are coordination of muscle activity and tone, balance, electroreception, and some aspects of motor learning. It is highly developed in electroreceptive aquatic nontetrapods and in birds and mammals.

Cerebral aqueduct (of Sylvius) Opening through which the third ventricle is connected with the fourth ventricle.

Cerebral hemispheres Paired structures that form the telencephalon; in mammals this term refers to the neocortical lobes (frontal, parietal, temporal, and occipital), the basal ganglia, septum, and related structures on each side.

Cerebrum See Telencephalon.

Cervical Refers to the neck region of the spine; may be used to indicate vertebrae, nerves or spinal cord segments.

Chemoreceptor Sensory receptor that responds to stimulation by specific classes of chemical compounds or components.

Chondrichthyes Cartilaginous fishes, comprising Elasmobranchi (sharks, skates, and rays) and Holocephali (ratfishes).

Chondrostei The sturgeons and paddlefishes: one of the five radiations of ray-finned fishes.

Chordates Group of deuterostome animals that have a notochord, comprising urochordates (tunicates), cephalochordates (lancelets), and vertebrates.

Clade A monophyletic set of taxa of any extent.

Cladistia The reedfishes or bichirs: the most basal of the five radiations of ray-finned fishes.

Cladistics A method of analysis for classifying animals according to their inferred phyletic relations based on sets of shared similar traits and/or for determining the polarity of a given trait based on its distribution within a set of phyletic relationships derived from traits unrelated to the trait being analyzed.

Cladogenesis See Speciation.

Cladogram A branching diagram that expresses phylogenetic relationships of a set of monophyletic taxa.

Clupeomorpha Taxon that includes herrings and anchovies: one of the four radiations of teleost fishes.

Coelacanth See Actinistia.

Colliculus Plural: Colliculi. One of four structures (arranged as two pairs: superior and inferior) that form the roof of the midbrain in mammals. Also see Tectum and Collothalamus.

Collothalamus Set of dorsal thalamic nuclei that receive their predominant input from the midbrain roof.

Column A longitudinally oriented group of axons, such as the dorsal column of the spinal cord; also see Fiber bundle. Also, a longitudinally oriented group of neuron cell bodies, such as the somatic efferent columns.

Commissure A group of axons that crosses the midline of the brain or spinal cord and terminates in the same area on the contralateral side. Some commissures, such as the posterior commissure, also contain decussating axons. Also see Decussation.

Contralateral On the opposite side of the brain or body.

Convergence An evolutionary process that produces homoplasy in distantly related taxa.

Corpus callosum Large bundle of commissural axons that interconnects the cerebral cortex in eutherian mammals.

Cortex Parts of the brain in which the neuron cell bodies are organized in a layered manner, such as in the cerebellum and the mammalian cerebral cortex.

Cranial nerves Set of nerves that emerge from the brain, in contrast to the spinal nerves that emerge from the spinal cord.

Craniates Taxon that includes cyclostomes (hagfishes and lampreys) and gnathostomes; with the revised taxonomic position of hagfishes as monophyletic with lampreys in the cyclostome clade, craniate is now a synonym of vertebrate.

Crossopterygian Refers to two groups of sarcopterygian fishes, one that comprises the coelacanth *Latimeria chalumnae* and the other that comprises the rhipidistian fishes, which were ancestral to tetrapods. Also see Actinistia.

Cyclostomes Jawless fishes, also called agnathans. Extant cyclostomes are the monophyletic group of lampreys and hagfishes.

Decussation A group of axons that crosses the midline and connects different structures on the two sides. Some decussations also contain commissural axons. Also see Commissure.

Dendrites The multiple processes of a neuron that receive afferent synapses from the axons (or dendrites) of other neurons.

Derived character See Apomorphy.

Deuterostomes Group of coelomate animals that comprise multiple groups including Echinodermata (which include star fishes and sea urchins), Hemichordata (acorn worms and pterobranchs), and Chordata (urochordates, cephalochordates, and vertebrates).

Diapsids Includes all extant reptiles and birds; the diapsid skull has two temporal fenestrae and two arches of bone. The ancestrally two fenestrae and arches have been lost in extant turtles and substantially modified in lizards, snakes, and birds.

Diencephalon The caudal part of the prosencephalon, or forebrain; comprises the epithalamus, dorsal thalamus, ventral thalamus (subthalamus), hypothalamus, pretectum, and posterior tuberculum.

Dipnoi Lungfishes: one of the three extant radiations of sarcopterygians.

Dorsal facial nerve Division of the seventh cranial nerve (VII_D) that innervates facial muscles and glands.

Dorsal glossopharyngeal nerve Division of the ninth cranial nerve (IX_D) that innervates the pharynx and salivary glands.

Dorsal root One of the two roots of spinal nerves (see also Ventral root); consists mostly of incoming sensory axons that enter the spinal cord on its dorsal side.

Dorsal root ganglion An aggregation of cell bodies of incoming sensory axons located on the dorsal root of the spinal cord.

Dorsal vagus nerve Division of the tenth cranial nerve (X_D) that innervates the viscera of the thorax and abdomen, the larynx, and the pharynx.

Dorsal ventricular ridge Part of the pallium of the telencephalon in reptiles and birds that lies ventral to the more dorsal part of the pallium and comprises anterior and posterior parts; formed either by a laminar cell plate or by nuclear areas.

Dura mater Outer layer of the meninges (the membranous layers of connective tissue) that cover the brain and spinal cord in tetrapods.

Ectoderm The most superficial of the three germ layers formed in the gastrula stage of embryogenesis.

Efferent An axon that projects away from the central nervous system or away from a specific part within it.

Elasmobranchs Group of cartilaginous fishes that includes sharks, skates, and rays.

Electroreceptor Sensory receptor that responds to stimulation by weak electric fields.

Elopomorpha Taxon that includes tenpounders, tarpons, and eels: one of the four radiations of teleost fishes.

Endoderm The deepest of the three germ layers formed in the gastrula stage of embryogenesis.

Ependyma Epithelial lining of the ventricles of the brain and the central canal of the spinal cord.

Epiphyseal nerve Cranial nerve (E) that innervates the epiphysis.

Epiphysis Part of the epithalamus; comprises pineal and/or parapineal structures.

Epithalamus Dorsal-most part of the diencephalon, lying dorsal to the dorsal thalamus; comprises the habenular and related nuclei and the epiphysis.

Euteleostei The largest of the four radiations of teleost fishes.

Eutheria Placental mammals.

Evagination Process of embryological development in which the neural tube in the telencephalon (or elsewhere) expands laterally and dorsoventrally by bulging outward.

Eversion Process of embryological development in which part or all of the roof of the neural tube in the telencephalon thins, elongates, and bends outward laterally.

Evolution Change over time.

Extrasegmental Refers to axons or reflexes that involve more than one segment of the spinal cord.

Fasciculus A slender bundle of axons, such as the medial longitudinal fasciculus of the brainstem. Also see Fiber bundle.

Fenestra A small opening or window, as in the fenestra rotundua (round window) of the middle ear.

Fiber An axon.

Fiber bundle A group of axons; also variably called a tract, fasciculus, funiculus, or column.

Field A developmental region that gives rise to one or more structures in the adult; or a part of the brain, such as the frontal eye field or prerubral field; or an area in space or on the body surface in which stimulation activates a sensory receptor or neuron.

Fitness The degree to which a variant will be selected for.

Floor plate A group of cells in the midline of the neural plate induced by the underlying notochord.

Foramen Plural: Foramina. A perforation or opening.

Foramen of Magendie Single, median opening that, along with the paired foramina of Luschka, connect the fourth ventricle with the subarachnoid space.

Foramina of Luschka Paired set of openings that, along with the single foramen of Magendie, connect the fourth ventricle with the subarachnoid space.

Foramina of Monroe Paired openings through which the lateral ventricles of the telencephalic hemispheres are in continuity with the third ventricle of the diencephalon.

Forebrain See Prosencephalon.

Fourth ventricle Cavity present in the hindbrain and caudally continuous with the central canal of the spinal cord.

Funiculus A group of axons forming a white matter tract or column in the spinal cord. Also see Fiber bundle.

Ganglion Plural: Ganglia. A collection of neuron cell bodies. In vertebrates, most often refers to such collections outside the brain and spinal cord; sometimes refers to a collection of neuron cell bodies in the brain, such as the basal ganglia. In some invertebrates, the central nervous system is composed of a series of ganglia.

Gastrula Embryonic stage following the blastula and in which three germ layers of ectoderm, mesoderm, and endoderm are formed.

Genotype The genetic composition of an organism.

Ginglymodi Gars: one of the five radiations of ray-finned fishes.

Glia Nonneural, supporting cellular constituents of the nervous system.

Glomerulus A ball-like synaptic complex of axon terminals and dendrites, as in the cerebellar cortex and the olfactory bulb.

Gnathostomes Jawed vertebrates.

Grades An assemblage of taxa characterized by a general level of organization and ranked among other such assemblages through sequences of successive levels of organization. A grade is the unit of phyletic analysis, or anagenesis.

Gray matter Tissue within the central nervous system that is predominantly composed of neuron cell bodies and unmyelinated neuron cell processes.

Gustatory Refers to the sense of taste.

Gymnophionans Caecilians: one of the three extant groups of amphibians.

Gyrencephalic Having a telencephalon with a surface that consists of many folds or convolutions. Each fold is known as a gyrus (plural = gyri); the valley between adjacent folds is known as a sulcus (plural = sulci). See Gyrus.

Gyrus Plural: Gyri. Ridges of cerebral cortex in mammals.

Hair cell Sensory cell of octavolateralis system that contains one or more hair-like processes.

Halecomorphi One of the five radiations of ray-finned fishes, of which only one species, the bowfin *Amia calva*, is extant.

Hemichordates Group of chordate animals that comprise acorn worms (enteropneusts) and pterobranchs.

Heterostracans One of the ostracoderm groups of extinct jawless fishes.

Higher A much misused and conceptually abused term as applied in comparative neurobiology; occasionally used to refer to the more rostral and dorsal parts of the brain, as in "higher centers"; most commonly refers to the alleged superiority of a given species as defined by human values in a *scala naturae* context. This term is best not used at all.

Hindbrain See Rhombencephalon.

Hodological Refers to axonal pathways and connections in the central nervous system; derived from the Greek word *bodos*, which means way or road. (No etymological relation to the second author of this volume!)

Holocephali Group of cartilaginous fishes that comprises the ratfishes, or chimaeras.

Homeobox gene Also referred to as a homeobox-containing gene, or *Hox*. One of a number of genes that contain a highly conserved sequence of DNA nucleotide base pairs and that are involved in rostrocaudal patterning in a wide variety of invertebrate and vertebrate species.

Homology Relationship of traits found in some, most, or all members of a taxon where the presence of that trait or its precursor or its genetic basis can in principle be traced to a common ancestor; the specific nature of the homologous relationship must be stipulated, for example, as a discrete structure, a derivative of all or part of a developmental field, or a serially repeated, segmental structure. Different criteria apply to historical (phylogenetic) homology, biological homology, and generative homology (see Chapter 1).

Homoplasy (Adjective: homoplastic or homoplasious). Similarity of traits found in a group of taxa, either monophyletic or polyphyletic, not due to inheritance from a common ancestor of the phenotypic trait itself but to independent, similar evolutionary changes; as in the case of homology, the homoplastic relationship must be stipulated as to its nature. See Convergence.

Hypoglossal nerve Twelfth cranial nerve (XII); innervates the muscles of the tongue and syrinx.

Hypophysis Pituitary; comprises the adenohypophysis rostrally and the neurohypophysis caudally.

Hypothalamus Ventral-most part of the diencephalon; set of nuclei involved in functions that include many relating to maintenance of the internal milieu of the body, emotion, motivational states, and control of the autonomic nervous system.

Interneuron Gogli type II neurons, i.e., local circuit neurons, that remain internal to a neuronal population. A less common usage is for any neuron that lies in the central nervous system between a primary sensory afferent neuron and an effector (or motor) neuron.

Ipsilateral On the same side of the brain or body.

Isocortex See Neocortex.

Isthmus A narrowing or constriction; most commonly refers to the caudal part of the mesencephalon where the brainstem narrows.

Intrasegmental Refers to axons that remain within a given segment of the spinal cord.

Lagena A flask-like evagination of the sacculus that contains auditory receptors.

Lateral line system An electroreceptive and/or mechanoreceptive sensory system present in many aquatic vertebrates.

Lateral ventricle Cavity present in each of the telencephalic hemispheres.

Lemniscal Refers to sensory pathways that ascend directly to the thalamus. See Lemnothalamus.

Lemnothalamus Set of dorsal thalamic nuclei that receive their predominant input directly rather than via a relay through the midbrain roof.

Lepidosaurs One of the two groups of diapsids; includes the Rhynchocephalia that comprises a single species, the tuatara *Sphenodon*, and the Squamata—the lizards, amphisbaenians, and snakes. Recent findings indicate that this is not a monophyletic taxon.

Limbic system Group of structures that encompasses the limbic lobe (hippocampal formation, cingulate gyrus, parahippocampal gyrus, and related cortices) and its related subcortical structures, including the amygdala, septal nuclei, and related parts of the striatum and diencephalon. This system plays important roles in emotion and memory.

Lissencephalic Having a telencephalon with a smooth surface that lacks sulci or gyri. See Gyrencephalic.

Lower A much misused and conceptually abused term as applied in comparative neurobiology; occasionally used to refer to the more ventral and caudal parts of the brain, as in the "lower brainstem"; most commonly refers to the alleged inferiority of a given species as defined by human values in a *scala naturae* context. This term is best not used at all.

Lumbar Refers the caudal region of the spine between the thoracic and sacral levels; may be used to indicate vertebrae, nerves, or spinal cord segments.

Mammals Amniotes with mammary glands and hair; includes monotremes, marsupials, and eutherians. See Synapsids.

Marsupials Metatherian mammals: mammals with pouches in which embryological development is completed.

Medulla Also known as medulla oblongata. Most caudal region of the brain, situated between the pons and the spinal cord. Location of many cranial nerve sensory and motor nuclei, reticular formation, and ascending and descending axonal pathways.

Meninges Singular: Meninx. A system of membranes that surrounds the central nervous system.

Mesencephalon Midbrain; lies caudal to the prosencephalon (forebrain) and rostral to the rhombencephalon (hindbrain). Comprises the tectum, midbrain tegmentum, and isthmus.

Mesoderm The middle of the three germ layers formed in the gastrula stage of embryogenesis.

Mesomeres Rostrocaudal segments of the mesencephalon formed during embryological development.

Mesozoic era Geologic time from 230 to 65 million years ago, divided into the Triassic period of 230 to 181 million years ago, the Jurassic period of 181 to 135 million years ago, and the Cretaceous period of 135 to 65 million years ago.

Metatheria Marsupials: one of the three radiations of mammals. See also Marsupials.

Metencephalon Rostral part of the hindbrain; comprises the cerebellum and, in mammals, the pons.

Midbrain See Mesencephalon.

Middle lateral line nerve One of three postotic lateral line cranial nerves (LL_M).

Monophyletic Pertaining to taxa that have all evolved from a single ancestral taxon.

Monotremes Prototherian mammals; egg-laying mammals. See also Prototheria.

Myelencephalon Caudal part of hindbrain; the medulla oblongata.

Myelin A white, fatty sheath surrounding some axons and, in rare instances, dendrites.

Myomere Muscle segment.

Myotome Embryonic muscle segment.

Neocortex Six-layered cortex that forms the largest part of the pallium in mammals; also known as isocortex.

Neoteny The retention of juvenile somatic characters in a reproductively mature individual.

Neural crest A group of cells that initially lie between the neural tube and the surface ectoderm. These cells form a variety of tissues, including sensory and postganglionic neurons, the visceral skeleton, and pigment cells.

Neural plate Thickened ectodermal tissue overlying the roof of the archenteron.

Neural tube Structure formed by folds of the neural plate that grow dorsally to meet and then fuse into a tube of neural tissue with a central lumen during embryological development.

Neuromasts Sensory hair cells of the lateral line system.

Neuromeres Embryonic, rostrocaudal segments of the brain.

Neuromodulators Chemical substances that act on a presynaptic membrane to alter the release of neurotransmitters or on postsynaptic membranes to change their sensitivity to neurotransmitters.

Neuron A nerve cell; a cell that transmits information by changes in polarization of parts of its membrane.

Neuropil A region with few or no neuron cell bodies in which neuron cell processes (axons and dendrites) are densely intertwined.

Neurotransmitters Chemical substances released by the presynaptic neuron at synaptic sites (or at a distance from them) that diffuse to postsynaptic receptor sites and affect the degree of polarization of the membrane of the postsynaptic neuron.

Notochord Rostrocaudally oriented structure of mesodermally derived cells ventral to the neural plate and/or neural tube; present in the adults of some invertebrate chordates and in the embryos and some adults of vertebrates.

Nucleus In the context of neuroanatomy, a group of neuron cell bodies within the central nervous system of vertebrates; also used in the context of cell biology to refer to an organelle within a cell body that contains the chromatin material.

Obex Small area overlying the caudal part of the fourth ventricle at the point where the fourth ventricle is continuous with the central canal that continues through the caudal medulla into the spinal cord.

Ocellus Plural: Ocelli. A simple eye consisting of one or a few pigmented receptor cells and associated cell(s).

Octaval nerve Eighth (ventibulocochlear) cranial nerve (VIII); cranial nerve that innervates the cochlear and vestibular organs.

Octavolateralis system The auditory, vestibular, and lateral line systems of fishes and larval amphibians; also called the acousticolateralis system.

Oculomotor nerve Third cranial nerve (III); one of three cranial nerves that innervate eye muscles.

Olfactory Refers to the sense of smell.

Olfactory bulb Paired structure at the rostral end of the telencephalon that receives afferent olfactory, or smell, input from receptor cells in the nasal mucosa and projects to olfactory regions of the telencephalon.

Olfactory nerve First cranial nerve (I); cranial nerve that innervates the olfactory epithelium.

Ommatidium A photosensitive unit of the compound eyes of arthropods.

Ontogeny Embryological development.

Optic chiasm Point of decussation of optic nerve axons to the contralateral side of the brain.

Optic nerve Second cranial nerve (II); cranial nerve that innervates the retina. This term is used for the portion of the optic nerve axons that lie distal to the optic chiasm.

Optic tectum Also known as the superior colliculus in mammals; part of the tectum (or roof) of the midbrain that predominantly receives visual and somatosensory information.

Optic tract Portion of the optic nerve axons that continue centripetally past the optic chiasm.

Organ of Jacobson See Vomeronasal organ.

Ostariophysi Large taxon of euteleosts that includes carp, goldfishes, minnows, catfishes, and piranhas.

Osteoglossomorpha Taxon that includes arawanas, arapaimas, notopterids, and mormyrids: the most basal of the four radiations of teleost fishes.

Otic lateral line nerve One of three preotic lateral line cranial nerves (LL₀).

Paedomorphism Retention of juvenile characters in the adult.

Paleozoic era Geologic time from 405 to 230 million years ago, divided into the Devonian period of 405 to 345 million years ago, the Carboniferous period of 345 to 280 million years ago, and the Permian period of 280 to 230 million years ago.

Pallidum Two components of the striatopallidal complexes in the striatum, or basal forebrain. In mammals, the dorsal pallidum is the globus pallidus, and the ventral pallidum consists of globus pallidus-like neurons within the substantia innominata.

Pallium The dorsal part of the telencephalon, with cytoarchitecture that is either solely cortical (see Cortex) or a combination of cortical and nuclear.

Parallelism The independent gain of the same phenotypic character in relatively closely related taxa.

Paraphysis Part of the epithalamus; closely associated with the epiphysis. May be glandular or photoreceptive.

Parasympathetic division of the autonomic nervous system See Autonomic nervous system.

Paraxial mesoderm Mesoderm that lies lateral to the neural tube during embryological development and forms somites and somitomeres in the head region.

Periventricular matrix Germinal cell layer immediately adjacent to the ventricular surface.

Phenotype The observable traits of an organism; the observable expression of the genotype.

Pheromones Chemical compounds used as social signals, such as for attraction of mates, marking of territories, and alerting members of the same species to danger.

Photoreceptor Sensory receptor that responds to stimulation by photons.

Phyletic evolution Process by which a single lineage, without branching into divergent lineages, undergoes change over time. See also Anagenesis.

Phyletic studies Studies that attempt to reconstruct the evolutionary history of a particular trait in a given lineage.

Phylogenetic scale See *Scala naturae*.

Phylogenetic tree Diagram of evolutionary relationships among taxa in which the location of each taxon indicates only the relative time of its appearance in the fossil record.

Phylogeny The evolutionary history of a taxon or taxa.

Pia mater Innermost of three membranous layers of connective tissue that cover the brain and spinal cord in mammals and birds.

Placode Area of thickened, neurogenic ectoderm in the developing head.

Plesiomorphy Adjective: Plesiomorphic. Traits that are present in a taxon or set of taxa that are similar to the respective primitive traits present in the common ancestral taxa;

for example, mammary glands and hair are *plesiomorphic* for mammals in that they were present in the common ancestral stock of all extant mammals. See also Apomorphy.

Polyphyletic Pertaining to a set of taxa that have evolved from more than one ancestral taxon.

Pons Region of the brain situated between the medulla and the midbrain. Location of many cranial nerve sensory and motor nuclei, reticular formation, and ascending and descending axonal pathways.

Posterior lateral line nerve One of three postotic lateral line cranial nerves (LL_p).

Posterior tuberculum Ventral, caudal part of the diencephalon; set of nuclei involved in a variety of pathways, including some visuomotor pathways and relay pathways to the telencephalon for the gustatory and lateral line systems.

Postganglionic axon An axon of the autonomic nervous system that originates in a sympathetic or parasympathetic ganglion and terminates on smooth muscles or glands. See Autonomic nervous system and Preganglionic axon.

Preganglionic axon An axon of the autonomic nervous system that terminates in a sympathetic or parasympathetic ganglion. See Autonomic nervous system and Postganglionic axon.

Preteetum Dorsal, caudal part of the diencephalon; set of nuclei involved in visuomotor and other functions.

Primitive Early, that is, relatively early in occurrence in the phylogenetic history of a line of descendant species. Sometimes used to mean simple or rudimentary.

Primitive meninx Single layer of membranous connective tissue that covers the brain and spinal cord in fishes.

Profundus nerve Cranial nerve (P) that innervates the skin of the snout; called the ophthalmic branch of the trigeminal (V) cranial nerve in mammals.

Projection Verb: Project. Refers to the group of axons that arises in a given neuron cell group and terminates in another neuron cell group, such as the projection of the retinal ganglion cells to the optic tectum or that the optic tectum projects to a nucleus in the dorsal thalamus. Also see Fiber bundle.

Proprioception Sense of position of the body and limbs derived from sensory receptors in muscles, tendons, and joints.

Prosencephalon The forebrain; lies rostral to the midbrain, or mesencephalon; comprises the telencephalon and diencephalon.

Prosomeres Rostrocaudal segments of the prosencephalon formed during embryological development.

Prototheria Monotremes—the platypus and echidnas: one of the three radiations of mammals.

Punctuated equilibrium Evolutionary pattern of maintenance of a given form for a long period of time followed by a short period of rapid change. See also Saltatory.

Ramus A branch of a nerve, such as a spinal nerve.

Ray-finned fishes See Actinopterygians.

Receptive field The area of the body or space in which stimulation activates a sensory neuron or receptor.

Reptiles Nonavian diapsids; includes squamates (lizards, snakes, and amphisbaenians), the tuatara *Sphenodon*, turtles, and crocodiles. See also Diapsids.

Reticular formation A coordinating system of neuronal populations located in the brainstem and spinal cord that has multiple functions, which include coordination of reflexes and the generation of motor patterns (descending reticular formation), as well as sleep, arousal, and attention (ascending reticular formation).

Retina Neuronal layer of the eye containing a complex neural network that includes photoreceptors, bipolar cells, and ganglion cells.

Retinotopic organization See Topographic organization.

Retrograde The direction away from the axonal terminal area and toward the dendrites.

Reversal An evolutionary process of alternate gain, loss, regain, etc. of a phenotypic character within a lineage over time.

Rhinal Refers to the nose, as in rhinal fissure or rhinencephalon.

Rhipidistians Group of sarcopterygian fishes that were the ancestral stock of tetrapods.

Rhombencephalon The hindbrain; lies caudal to the midbrain, or mesencephalon; comprises the metencephalon and myelencephalon.

Rhombomeres Rostrocaudal segments of the rhombencephalon formed during embryological development.

Sacculus Bag-like chamber of the vestibular apparatus of the inner ear.

Sacral Refers to the most caudal region of the spine; may be used to indicate vertebrae, nerves, or spinal cord segments.

Saltatory Refers to sudden or abrupt change or leap, as in a rapid evolutionary change with the abrupt establishment of new species. See also Punctuated equilibrium.

Sarcopterygians The subclass of Osteichthyes, or bony fishes, that comprise the fleshy-finned fishes, which include coelacanth, rhipidistians, and lungfishes, and which ancestrally gave rise to tetrapods.

Sauropsid The clade of reptiles and birds; with the revised taxonomic position of turtles, sauropsid is now synonymous with diapsid.

Scala naturae Scale of nature. Idea that animals can be ranked along a progressively ascending scale that is defined by human values and with humans ranked at the top.

Secondary meninx Inner of two membranous layers of connective tissue that cover the brain and spinal cord in amphibians and reptiles.

Segment One of a series of repeating, similar, rostrocaudally arrayed, morphological units.

Serial homologues Similar, segmentally repeating structures in the body of an individual, such as vertebrae. Sometimes referred to as iteration.

Sexual dimorphism A difference between males and females in the structure or appearance of a body part.

Somatic Refers to musculoskeletal structures that develop in the body wall from mesoderm, as opposed to derivatives the gut (endoderm) or of the body surface (ectoderm).

Somatotopic organization See Topographic organization.

Somites Rostrocaudal segments of the paraxial mesoderm that lie lateral to the neural tube in the trunk and caudal part of the head during development.

Somitomeres Rostrocaudal, incompletely separated segments of the paraxial mesoderm that lie lateral to the neural tube in the rostral part of the head during development.

Speciation Also called Cladogenesis. Process in which a single species gives rise to one or more new sister species or to two or more lineages of new species.

Species A group of naturally interbreeding or potentially interbreeding individuals that do not naturally breed with individuals outside of the group.

Spinal accessory nerve Eleventh cranial nerve (XI); innervates neck and shoulder muscles.

Squamates Order of reptiles that comprises lizards, snakes, and amphisbaenians.

Striatum Two areas within the striatopallidal complexes in the basal forebrain; in mammals, the dorsal striatum is the caudate nucleus and putamen, and the ventral striatum is the olfactory tubercle and nucleus accumbens.

Sulcus Plural: Sulci. Valleys between the gyri (ridges) of the cerebral cortex in gyrencephalic mammals; particularly deep sulci are referred to as fissures.

Suprasegmental Refers to axons or reflexes that involve the brain in addition to the spinal cord.

Supratemporal lateral line nerve One of three postotic lateral line cranial nerves (LL_{ST}).

Sympathetic division of the autonomic nervous system See Autonomic nervous system.

Synapse A specialized region of part of an axon (or dendrite) that transmits information to the receptive part of another neuron by release of neuroactive substances or electrotonically.

Synapsids Includes modern mammals; the synapsid skull has a single temporal fenestra, or opening.

Taxon Plural: Taxa. A unit of classification of organisms, for example, a species, a genus, a class, a kingdom.

Tectum Roof, or dorsal part, of the mesencephalon, or mid-brain; comprises the optic tectum (superior colliculus), torus semicircularis (inferior colliculus), and, in ray-finned fishes, the torus longitudinalis.

Tegmentum Ventral part of the mesencephalon, or mid-brain.

Telencephalon Rostral part of the prosencephalon, or fore-brain; comprises the pallium and subpallium.

Teleostei The largest of the five radiations of ray-finned fishes.

Terminal nerve Also called nervus terminalis; cranial nerve (T) that innervates the nasal septum and, in ray-finned fishes, projects to the retina.

Tetrapods Vertebrates with four feet, whether the feet are retained or have been secondarily lost or modified. Synonym of quadruped.

Thalamus, dorsal Part of the diencephalon, lying ventral to the epithalamus and dorsal to the ventral thalamus; set of nuclei that relay information to the telencephalon.

Thalamus, ventral Part of the diencephalon, lying ventral to the dorsal thalamus and dorsal to the hypothalamus; set of nuclei, some of which are involved in motor and visual pathways.

Thecodonts The taxon of diapsids that comprises crocodiles and birds.

Therian Subclass of mammals that comprise metatherians (marsupials) and eutherians (placental mammals).

Third ventricle Midline cavity present in the diencephalon; contains cerebrospinal fluid.

Thoracic Refers to the region of the spine between the cervical and lumbar levels; may be used to indicate vertebrae, nerves, or spinal cord segments.

Tonotopic organization See Topographic organization.

Topographic organization The preservation of the spatial organization present on a receptor surface, such as the skin (somatotopic) or the retina (retinotopic), or of frequency in the cochlea (tonotopic), in neuronal populations of the central nervous system, such as the somatosensory cortex, the lateral geniculate nucleus, or the auditory cortex.

Topological Refers to those spatial relationships among components of the nervous system that are independent of size and shape; these include sequential relationships and whether one component is contained within another.

Torus lateralis Present only in ray-finned fishes; a lateral part of the tegmentum of the midbrain.

Torus longitudinalis Present only in ray-finned fishes; part of the tectum (or roof) of the midbrain.

Torus semicircularis Also known as the inferior colliculus in mammals; part of the tectum (or roof) of the midbrain that receives auditory input and, where present, lateral line input.

Tract A group of axons. See also Fiber bundle.

Trigeminal nerve Fifth cranial nerve (V); supplies motor innervation to jaw muscles and sensory innervation to the face, snout, and oral cavity.

Trochlear nerve Fourth cranial nerve (IV); one of three cranial nerves that innervate eye muscles.

Tunicate The basal invertebrate chordate group, also known as urochordates.

Urochordates Group of chordate animals that comprise tunicates, which includes the ascidians, or sea squirts. Also see Tunicate.

Urodeles Newts or salamanders: one of the three extant groups of amphibians. Also called Caudata in reference to the presence of a tail.

Ventral root One of the two roots of spinal nerves (see also Dorsal root); consists mostly of motor axons that exit the spinal cord from its ventral side.

Ventricles Chambers or cavities: set of cavities in the brains of vertebrates that contain cerebrospinal fluid and are continuous with the central canal of the spinal cord; also chambers within the heart.

Ventrolateral facial nerve Division of the seventh cranial nerve (VII_{VL}) that innervates taste buds.

Ventrolateral glossopharyngeal nerve Division of the ninth cranial nerve (IX_{VL}) that innervates taste buds.

Ventrolateral vagus nerve Division of the tenth cranial nerve (X_{VL}) that innervates taste buds.

Vertebrae Set of repeating, segmental, bony units that form the vertebral column, or backbone.

Vertebrates Group of chordate animals that have (or had ancestrally) vertebrae, that is, backbones. Extant members are the cyclostomes (hagfishes and lampreys) and the gnathostomes. See also Craniates.

Vestibulocochlear nerve See Octaval nerve.

Visceral arches Series of skeletal arches that support the gills in fishes; the first visceral arch is the mandibular arch, the second is the hyoid arch, and the third through seventh visceral arches are the first through the fifth branchial arches.

Vomeronasal nerve Cranial nerve (VN) that innervates the vomeronasal organ.

Vomeronasal organ Accessory olfactory organ typically used for detection of pheromones. Present in many tetrapods. Also called the Organ of Jacobson.

White matter Tissue within the central nervous system that is composed of myelinated axons.

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Index

Note that this index contains a mixture of Latin, English, and other language terms for nuclei, tracts, and other structures. As in the text, we have presented the names of the structures here as we have variously encountered them in most of the English-based literature that we surveyed, rather than following the *Nomina Anatomica* system of Latin names. In this literature, some terms, such as *ansa lenticularis* and *substantia nigra*, most frequently appear in Latin or other non-English language, while others, such as *red nucleus* and *lateral ventricle*, most frequently appear in English. Other terms, such as *visual Wulst*, are a mixture of languages, and still others appear either in English or in other languages with about equal frequency, such as *brachium conjunctivum/superior cerebellar peduncle*. Just as one deals with the variation in the languages of these terms in the literature, we hope that the reader will be able to deal with the similar mix contained herein. This index includes page listings for many of the structures as they appear in various figures as well as in the body of the text itself.

The reader is also referred to the Glossary for definitions of a number of the terms used in the text, as well as to the Contents for specific subjects and the relevant structures discussed therewith. Note that while many nuclei are listed by their name directly under the heading Nucleus, a number are listed under their own name, such as Preglomerular nuclear complex, under their regional designation, such as Nucleus, preoptic(us); Nucleus, pretectal(is); Hypothalamus; Arcopallium; Mesopallium; and Nidopallium, or under alternative headings such as Area, Complex, Reticular formation, or Substantia.

Finally, please note that, for the most part, authors are cited here only for direct mention in the body of the text. Authors cited in figure captions, references at the end of each chapter, or in the text boxes generally are not included in this index.

Aardvarks, 559–560

Abneural surface, *see* Surface, abneural

Accessory:

olfactory bulb, *see* Olfactory, accessory bulb

optic system, 344, 373, 375, 389–396, 398

Acetylcholine/cholinergic and/or Acetylcholinesterase (AChE), *see also* Choline acetyltransferase (CHAT).
24–25, 141, 230, 232–233, 235, 255, 272, 281,
283–284, 320, 352, 364, 367–369, 462–463,
471–474, 476–477, 480, 482, 484, 488–489, 626,
629

Acorn worms, *see* Hemichordata/es

Actinistia, *see* Crossopterygian and *Latimeria*

Actinopterygians:

brain size, 101–102

evolution, 96

general listing, 41, 58, 73–74, 76–77, 84, 86–89, 131, 133,
141, 185–186, 188, 190, 192–197, 210–213, 216,
274, 343, 350, 364, 369, 407–408, 410,
413–414, 450–451, 453, 472, 488–489, 495, 499,
501, 611, 654–655

nonteleosts, *see also* Cladistia, Chondrostei, Ginglymodi, and
Halecomorphi, *as well as individual listings,*
such as sturgeon, or genus names, such as
Polypterus and Amia. 275, 281, 283, 285, 290,
292–294, 303–305, 312, 315–316, 318, 334–335,
344, 352–353, 375–376, 380, 391, 395–396, 418,
421, 427, 432, 473–474, 477, 496–497, 499–500,
611–613, 628–629, 653

teleosts (including Euteleostei), *see also* Osteoglossomorpha,
Elopomorpha, and Clupeomorpha, *as well as*
individual listings, such as Goldfish and Trout,
or genus names, such as Carassius and Danio.
34, 76, 78, 137, 141, 144, 245, 275–276,
280–281, 283–285, 290, 292, 295, 298, 304–305,
319, 322–325, 334–335, 378, 383, 391–399, 407,
410, 413–414, 417, 423, 430, 434, 477,
497–501, 611, 613, 615–616, 629, 650, 653–655,
658

term, 74, 76–77, 86

Adaptation:

behavioral, 93, 100

general aspects, 93–95

sensory, 30

Additions, terminal, 60

Adenohypophysis:

dorsal lobe, 446–447

general aspects, 446, 448, 453, 457, 460

hormones, *see* Hormones, anterior pituitary

pars distalis, 446

pars infundibularis, *see* Adenohypophysis, pars distalis

pars intermedia, 446, 457

pars tuberalis, 446

ventral lobe, 446–447

Adrenal gland, *see* Gland(s), adrenal

Adrenaline, *see* Epinephrine

Adrenocorticotrophic hormone (ACTH), 25–26

Agnatha/ns (Cyclostomes), *see also* Hagfishes and Lampreys.

73–75, 84, 86, 88, 101–102, 128, 133, 141, 144,
451, 644, 654

- Aldridge, R. J., 644
 Alex (African gray parrot), 516
Alligator, 33, 362
 Alligators, *see* Crocodiles
 Allman, J., 118, 505
 Allocortex, *see also* Hippocampus *and* Cortex, olfactory. 353
 Allodendrites, 22–23
 Allopheny, 12–13
 Allometry, *see* Brain, allometry
 Alveus, *see* Tract, alveus
 Ambulacraria, 49, 638, 644, 646
Ambystoma, 87, 196
Amia, 76–78, 87–88, 197, 304–305, 312, 315, 318, 349–350, 375–376, 380, 391, 395–396, 410, 413, 421, 454, 497
 Amines, biogenic, 25
 Amino acids, 25, 28
 Ammocoete, 75
 Ammon's horn, *see* Hippocampus, Ammon's horn
 Amniotes, term, 73, 80–82, 86
 Amphibian(s), *see also* Anurans, Gymnophionans, *and* Urodeles, *as well as individual genus names, such as Rana and Xenopus*.
 evolution of, 136
 general listing, 41, 78, 81–82, 86, 88, 96, 101, 106, 141, 190, 228–229, 275, 278, 290, 292, 294, 303–305, 312–313, 319–322, 324, 329, 332–335, 349–350, 353–354, 364, 375, 377, 391, 396, 407–410, 414, 418–419, 422, 427, 430, 432–433, 437, 446–447, 450, 455, 474–476, 488–489, 497–498, 501, 575, 595, 603, 611–614, 625, 628, 630, 653, 656
 papilla, *see* Papilla, amphibian
Amphioxus/Amphioxus, *see* Branchiostoma
 Ampulla caudalis, 145
 Ampullae of Lorenzini, *see* Receptors, electrosensory
 Amun Kneph, 618
 Amygdala, *see also* Formation, claustroramygdalar.
 anterior area (of mammals), 366
 archistriatum (of birds), *see* Arcopallium
 area subpallialis amygdalae (SpA) (of birds), 348, 511
 autonomic division (central nucleus) (of mammals), 359–360, 365–367, 487, 546, 601, 603
 basal division (of mammals), *see* Amygdala, frontotemporal division (of mammals)
 basolateral division (of mammals), *see* Amygdala, frontotemporal division (of mammals)
 cortical division (of mammals), *see* Amygdala, olfactory divisions (of mammals)
 corticomedial division (of mammals), *see* Amygdala, olfactory divisions (of mammals)
 dorsolateral (of squamates), 511
 extended, 359, 364–365, 367, 369, 488, 511
 frontotemporal division (of mammals), 119–120, 359–360, 366, 487, 495, 499, 504, 523, 537, 611, 616, 620, 622, 655
 general aspects, 66, 233–234, 300, 305, 343, 355, 358–359, 361–362, 365, 411, 430, 433, 435, 450, 455–456, 460, 474, 482–483, 488, 495, 501–502, 551, 594–595, 600, 603, 611, 616–618, 622, 626, 629–630, 657
 nucleus:
 anterior area (of amphibians), *see* Area, anterior amygdalar
 basolateral (of mammals):
 anterior basolateral, 359–360
 general aspects, 359–360, 487, 504, 511, 601
 posterior basolateral, 360
 basomedial (anterior and posterior), (of mammals), 360, 601
 central:
 of amphibians, 354, 475, 488
 of mammals, *see also* Amygdala, autonomic division (of mammals). 359–360, 487–489
 cortical (of mammals), 360, 600–601, 603
 external (of reptiles), 601
 lateral:
 of amphibians, 353–354, 475, 488, 497–498, 612–613
 of mammals, 305, 333, 359–360, 420, 431–432, 487, 504, 508–509, 511, 540, 543, 537–538
 medial:
 of amphibians, 353–354, 475, 488, 612–613
 of mammals, *see also* Amygdala, olfactory divisions (of mammals). 358, 487–489, 511
 of reptiles, 488, 604
 pars lateralis (of amphibians), 603
 pars medialis (of amphibians), 603
 posterior (of mammals), 360, 601
 posterior (of reptiles) (PDVR), 601
 posterioris amygdalopallii (PoA) (posterior pallial amygdala) (of birds), 348, 511
 sphericus (of squamates), 362, 457, 504, 601, 603–604
 taeniae:
 amygdalae (TnA) (of birds), 348, 488, 511, 629
 of teleosts (NT), 500, 598, 615, 629
 ventral anterior (of reptiles), 601
 vomeronasal, *see* Amygdala, nucleus sphericus *and* Amygdala, olfactory divisions (of mammals)
 olfactory divisions (of mammals), 358–360, 362, 365, 367, 487, 501, 593, 600–601, 611, 616, 629
 pallial, 593, 594
 piriform-amygdalar area, *see* Area, piriform-amygdalar
 postpiriform transition area, *see* Area, postpiriform transition
 striatal (subpallial), 359–360, 471, 488–489, 600–601, 604, 611
Anabas, 136
Anableps, 413
 Anagenesis, *see* Evolution, phyletic
 Analogy, 8, 11, 617
 Anamniotes, term, 73
 Anapsida/s, term, 80, 82
Anas, 217
 Anaspids, 75
 Angiotensin II, 25
 Anlage, *see* Field(s), morphogenetic
 Annelida/s, 638
Anolis, 151
 Anophthalmia, 651
 Ansa lenticularis, 478
Anser, 160
 Anteaters:
 edentate, 205, 303
 spiny, *see* Echidnas
 Anterior, term, 665–667
 Anurans, 78–79, 95–97, 131, 138, 205, 244, 246–247, 275, 278, 281, 285, 290, 294, 303–305, 319–322, 324, 332–333, 335, 349–350, 353–354, 375, 377, 409, 414, 418, 422, 427, 430, 432–433, 437, 448, 474–475, 489, 497–498, 575, 582, 586, 595, 597, 601, 603, 605, 612–614, 625
 Anus, 51, 638
 Apes, 96, 527, 534, 566

- Aphasia:
 Broca's, 587
 motor, *see* Aphasia, Broca's
 sensory, *see* Aphasia, Wernicke's
 Wernicke's, 587
- Apomorphy (Apomorphic), 13–14, 16
- Apoptosis, 151
- Apterotonotus*, 298, 305, 397
- Aqueduct, cerebral, of Sylvius, 67
- Arachidonic acid, 25
- Arachnoid:
 meninges, 66
 villi, 67
- Arantius, Julius Caesar, 618
- Archaeopteryx*, 103
- Archenteron, 49, 51–52, 647
- Arch(es):
 branchial, 159–160, 162, 168
 hyoid, 159–160
 mandibular, 159–160, 184
 visceral, 159–160, 162, 164–165, 168
 zygomatic, 524–525
- Archistrium, *see* Arcopallium
- anterior, *see* Arcopallium, anterior (AA)
- central nucleus of anterior, *see* Arcopallium, nucleus, centralis arcopallii anterioris (AAC) (in parrots)
- intermedium, *see* Arcopallium, intermedium (AD)
- intermedium, pars dorsalis, *see* Arcopallium, dorsale (AD)
- mediale, *see* Arcopallium, mediale (AM)
- nucleus taeniae, *see* Amygdala, nucleus, taeniae, amygdalae (TnA) (of birds)
- pars dorsalis, *see* Arcopallium, dorsale
- robust nucleus of, *see* Arcopallium, nucleus, robustus arcopallii
- ventral part, pars ventralis, plus caudal part, *see* Amygdala, nucleus, posterioris amygdalopallii (PoA)
- Archosauria, term, 80
- Arcopallium (A):
 anterior (AA), 348, 565
 cup, 585, 587
 dorsale (AD), 348
 general aspects, 348, 363, 388, 457, 507, 511, 561, 565, 581
 intermedium (AD), 348, 566, 585
 mediale (AM), 348
 nucleus:
 centralis arcopallii anterioris (central of anterior arcopallium) (AAC) (in parrots), 348, 584, 585
 robustus arcopallii (robust) (RA), 348, 511, 584–586, 589
- Area(s):
 anterior amygdalar (of amphibians), 475, 488, 603
 Broca's, 114, 357, 587–588
 Brodman's:
 1, 556
 2, 556–557
 3, 556
 4, 558
 5, 557, 559
 6, 558
 7, 557
 8, 558
 17, *see* Cortex, visual, areas
 18, *see* Cortex, visual, areas
 19, *see* Cortex, visual, areas
 22, 587
 24, 558, 587
 41, 577
 42, 577
 43, 429
 44, 587
 45, 587
 general aspects, 357
 central tegmental, 384
 c (of turtles), *see* Nucleus, accumbens, of turtles
 cortical:
 A1 and A2, *see* Cortex, auditory *and* Cortex, auditory belt dorsolateral (DL) (of mammals), 532, 543
 dorsomedial (DM) (of mammals), 532, 543
 M1, M2, and M3, *see* Cortex, motor
 S1 and S2, *see* Cortex, somatosensory
 V1, V2, etc., *see* Cortex, visual
 corticoidea dorsolateralis (dorsolateral corticoid) (CDL) (of birds), 348, 388, 510, 513–514, 516, 581
 d (of turtles), *see* Striatum, dorsal, of reptiles, of turtles *and* Nucleus, accumbens, of reptiles
 dorsal telencephalic (D) (of ray-finned fishes), *see also* Pallium, dorsolateral (of Cladistia) *and* Pallium, dorsomedial, of Cladistia.
 central zone of (Dc), 323, 334, 398, 498, 500–501
 dorsal zone of (Dd), 498–500, 599
 general aspects, 496, 499–501, 612–613, 615–617
 lateral zone of (Dl):
 dorsal part of (Dld), 499–500, 615
 general aspects, 434, 498–500, 616–617
 posterior part of (Dlp), 615
 ventral part of (Dlv), 499–501, 615–617, 629–630
 medial zone of (Dm), 193, 211–212, 397–398, 420, 430, 489, 498–501, 598–599, 613, 615–617
 posterior zone of (Dp), 193, 499–500, 598–599, 605, 613, 615–616
 entopeduncular, *see* Nucleus, entopeduncular
 lateral hypothalamic, 445, 448, 455, 457, 460–461
 lateralis of the posterior tuberculum (of hagfishes), 396
 L pallii, *see* Nidopallium, area L pallii
 medial hypothalamic (region), 455
 octavolateralis, 279, 295
 P1 (of Cladistia), *see* Pallium, dorsomedial (of Cladistia)
 P1-P5 (of hagfishes), *see* Pallium, P1-P5 (of hagfishes)
 P2-P3 (of Cladistia), *see* Pallium, dorsolateral (of Cladistia)
 parahippocampal(is) (of birds), *see* Hippocampus, parahippocampal area
 periventricularis ventrolateralis (of cartilaginous fishes), 364, 472–473, 476
 piriform-amygdalar, 360
 pontine taste, *see also* Nucleus, parabrachial. 190, 192–193
 postpiriform transition, 360
 preoptic, *see also* Nuclei, preoptic(us). 350, 352, 354, 366, 409–412, 445, 448, 450–455, 457, 460–461, 474–475, 501, 582, 595, 605, 613, 622, 629
 prerubral, 290
 pretectalis:
 of birds, 302, 387, 390, 395–396
 of monotremes, 380
 retrobrubral, 293
 septal, *see* Septum/Septal area
 strio-amygdaloid transition (of reptiles), 488
 subpallialis amygdalae, *see* Amygdala, area subpallialis
 superficialis basalis (of cartilaginous fishes), 354, 364, 472–473, 476
 temporo-parieto-occipital (TPO) (of birds), 348, 513–514, 564–565
 ventral(is):
 tegmental,

- of amniotes, general aspects, 233, 268–269, 273, 289, 292–293, 296, 300, 303, 344, 478
 - of birds, 268, 271, 282, 301–302, 484
 - of cartilaginous fishes, 291, 294–295, 297, 344, 489
 - of mammals, 299, 384, 411, 425, 482–483, 510, 623, 629
 - of reptiles, 301, 484
- telencephalic (V) (of ray-finned fishes):
 - general aspects, 211–212, 489, 500 (AVT), 613
 - nuclei of:
 - commissural (Vc), 477, 500, 598–599, 615, 629
 - dorsal (Vd), 410, 418, 430, 473–474, 477, 500, 613, 615
 - intermediate (Vi), 500, 598–599, 615, 629
 - lateral (VL), 474, 477, 489, 500
 - 'nother (Vn), 474, 500
 - postcommissural (Vp), 500, 598–599, 615, 629
 - supra commissural (Vs), 500–501, 596, 598–599, 605, 613, 615, 629
 - ventral (Vv), 212, 364, 369, 474, 477, 499–501, 598, 605, 613, 615–616, 628–629
 - of Tsai, 268
 - ventrointermediate (VIA) (of birds), 428, 431, 436, 438, 485–487, 565–566
 - visual:
 - dorsal (of reptiles), 541
 - dorsolateral (of reptiles), 540
 - ventral (of reptiles), 541
 - ventromedial (of reptiles), 540
 - Wernicke's, 587–588
 - X (of birds), 345, 584–586
- Arendt, D., 641
- Arginine vasotocin, *see* Vasopressin
- Ariëns Kappers, C. U., 69, 115
- Armadillos, 560
- Armstrong, J. A., 69
- Arthropoda/s, 162, 637–639, 641–642, 657–658
- Ascidia/ns, *see* Urochordata/es
- Astrocytes, *see* Glia, astrocytes *and* Glia, radial
- Atoji, Y., 626
- Attention, 221
- Autonomic nervous system:
 - craniosacral division, 462
 - enteric division, 461
 - general aspects, 63, 102, 129, 134, 179, 359–360, 460–463
 - parasympathetic division, 63, 129, 136, 148, 179, 205, 209–211, 215, 457
 - sympathetic:
 - chain (of ganglia), 129
 - division, 63, 129, 148, 179, 233, 409, 457
 - thoracolumbar division, 462
- Aves, term, *see also* Birds.
- Avian Brain Nomenclature Forum, *see also* Nomenclature, revised avian. 70, 268, 344, 504, 511
- Axis (direction):
 - dorsoventral, 54, 61, 641, 643, 645, 666–667
 - lateral-medial, 61
 - neural-abneural, 641, 643, 645
 - rostral-caudal, 50, 54, 61, 657, 666–667
- Axonal tracing techniques, *see* Neuronal tracing techniques
- Axonal transport, *see* Neuronal transport
- Axons:
 - afferent, term, 62–62
 - centrifugal, 36
 - collateral, *see* Collateral(s), branch
 - efferent, term, 62–63
 - general aspects, 20, 23–24, 62–63
 - giant, 131, 224
 - giant squid, 95
 - hillock, 142
 - Mauthner, 139–141, 143, 228
 - Müller, 139–141
 - postganglionic:
 - parasympathetic, 129
 - sympathetic, 129, 133, 462
 - preganglionic:
 - parasympathetic, 129
 - sympathetic, 129, 133, 152, 462
 - terminals, 20
- Axoplasmic transport, *see* Neuronal transport
- Baars, B. J., 507
- Baillargier, J., 531
- Baillargier, outer stripe of, 531
- Baker, R., 166
- Barbels, 38, 40, 44–45, 190
- Barrelettes, 556
- Barreloids, 556
- Barrels, somatosensory, 44–45, 355, 556
- Basal ganglia, term, *see* Ganglia/on, basal
- Basilar papilla, *see* Papilla, basilar
- Basis pedunculi, term, 289
- Bass, A. H., 118, 212
- Batoidea, term, *see also* Guitarfishes, Rays, *and* Skates. 76
- Bats, 96, 99, 104, 137–138, 303, 305–306, 553, 559–560, 572–573, 578–579, 587
- Beavers, 138, 560
- Beccari, N., 69
- Becker, T., 542
- Behavior(s):
 - adaptation, 100
 - aggression, 305, 450, 455, 460–461, 501, 629
 - arousal, 109
 - attack, 320–321
 - attention, 109, 136, 326, 505
 - chewing, 133
 - color change, 453
 - communication (including language), 144, 211–213, 304–305, 501, 516
 - complexity of, 107
 - copulatory, *see* Behavior, reproductive
 - courtship, 106, 305, 455
 - diving, 217
 - dreaming, *see* Dreaming
 - drinking, 232
 - drumming, 141
 - emotional, 109, 352, 504, 611, 622, 630
 - escape/predator avoidance, 106, 139, 141, 143–144, 320–321, 329, 655
 - feeding and swallowing, 99, 136, 207–211, 232, 284, 320–321, 352, 460–461, 448, 450, 457, 501, 649, 652, 655
 - flight, 146
 - grasping, 228, 262
 - jamming avoidance response, 213
 - learning:
 - general aspects, 501, 611, 623, 630
 - successive reversal, 514
 - vocal, 95, 457
 - locomotor, *see also* Locomotion. 105, 133–134, 137–138, 144, 146, 152, 623, 629
 - maternal (mother-infant bonding), 504

- memory, *see* Memory
 migratory, 188, 313
 motivational, 611, 630
 navigation, 43
 nest building, 501
 orientation, 43, 188, 313, 329, 380, 409
 parental, 445, 447, 450, 455, 461, 604
 pecking, 284, 561
 phototaxis, negative, 374
 predatory (predation)/prey-seeking, 106, 139, 144, 326, 649, 652, 655
 preening, 232
 prey capture, 320–321, 329, 375
 reasoning, 107
 reproductive, 106, 304–305, 352, 407, 448, 450, 455, 460, 488, 501, 604–605, 611
 rhythmic, 133–134, 137, 139, 221, 445
 scratching, 262
 sleep, *see* Reticular formation, and sleep *and* Sleep
 social, 106, 449–450, 461, 506, 655
 spatial mapping, 611, 627, 629, 639
 sweeping, 501
 temperature regulation, 352, 409, 451, 460–461, 548–549
 territorial defense, 106, 304–305
 visual discrimination, 330
 vocalization, 455, 457
 waking, *see* Wakefulness
- Belekhova, M., 332
 Bell, C., 258
 Bellonci, J., 69
 Beta(β)-endorphin, 25
 Bichirs, *see* Cladistia
 Bilateral, term, 666
 Bilateria, 637–639, 641–642, 644, 658
 Binaural difference, 572, 574
 Bingman, V. P., 627
 Biped(s):
 general aspects, 138
 term, 667
- Birds, *see also some individual listings, such as* Pigeons, Owls, *and* Parrots, *and genus names, such as* *Anas*, *Columba*, *and* *Larus*. 31, 79–81, 85–86, 88–89, 96, 101, 103, 105, 119–120, 131, 135, 137–138, 146–147, 152, 160, 164, 170, 184–185, 187–188, 190, 198–200, 205, 208–209, 211, 217, 228, 230, 237, 268, 271, 274–275, 278, 282–285, 290, 301–303, 305–306, 313, 322, 329–333, 335, 344, 350, 352, 361, 363–364, 368–369, 380, 385–388, 390–391, 394–396, 407, 409, 412, 419–420, 426, 428, 431–432, 436–439, 446–448, 450, 457, 472, 479–480, 483–489, 495, 501–502, 504, 507–515, 538, 559–563, 565–566, 576, 579, 581, 583–589, 601–603, 605–606, 617, 626–630, 654–658
- Bishop, G. H., 115–116
 Bladder:
 swim, 141, 211
 urinary, 461, 463
 Blastocoel, 49, 51
 Blastopore, 49, 51, 638
 Blastula, 49–51
 Blind mole rat, *see* Mole rats, blind
 Blood pressure, 233, 449–450, 453, 463
 Body:
 glycogen, 146–147, 150
 growth of, 448–449
 juxtarestiform, *see* Peduncle, cerebellar, inferior
 lamellar (of *Branchiostoma*), 647–649
 mammillary (of teleosts), *see* Nucleus, mammillary body, of teleosts
 mushroom:
 calyx of, 639
 general aspects, 639, 641
 restiform, *see* Peduncle, cerebellar, inferior
 Bombesin, 25
Bombina, 433
 Bone morphogenetic proteins (BMPs), 49, 54, 162
 Bones:
 alisphenoid, 160
 articular, 159–160, 213–214
 columella, 159–160, 213–214
 dermal, 159–160
 ethmoid, 40–41, 160
 exoccipital, 160
 incus, 159–160, 214
 malleus, 159–160, 214
 mandible, 160
 nasal, 160
 occipital, 160
 orbitosphenoid, 160
 ossicle(s), 159–160, 213–213
 otic, 160
 quadrate, 159–160, 213–214
 stapes, 159–160, 214
 supraoccipital, 160
 turbinate, 39, 41
 tympanic bulla, 160
 Bowfin, *see* *Amia*
 Bowsher, D., 115–117
 Brachium conjunctivum, *see* Peduncle, cerebellar, superior
 Brachium pontis, *see* Peduncle, cerebellar, middle
 Brady, J., 119
 Bradykinin, 25
 Braford, M. R., Jr., 118
 Brahic, C., 582
 Brain:
 allometry, 100–102, 109
 development, *see* Development (embryological)
 of dinosaurs, 103
 and intelligence, 93, 101, 106–109
 of invertebrates, *see* Invertebrate(s), central nervous system
 size (brain-body ratios), 100–106, 109, 515, 649, 651, 653
 triune, *see* Theory, triune brain
 volume, *see* Brain, size
 weight, *see* Brain, size
 Brainstem, term, 66
Branchiostoma (lancelet, amphioxus), 49, 73–75, 637, 644, 646–649, 651–653, 655
 Brenowitz, E. A., 516
 Brittijt, M. L., 344
 Broca, P. P., 587, 618
 Broca's:
 aphasia, *see* Aphasia, Broca's
 area, *see* Area(s), Broca's
 Brodal, A., 224
 Brodmann, areas, *see* Area(s), Brodmann's
 Brodmann, K., 357
 Broglio, C., 499, 616
Brontosaurus, 103
 Bruce, L. L., 119–120, 512
 Budgerigar, 585

- Bulb, olfactory, *see* Olfactory, accessory *and* Olfactory, main
- Bullfrog, *see* *Rana*
- Bulls, 98, 249–250
- Bundle(s), *see also* Tract(s/us) and Pathway(s).
- Bagley's, *see also* Tract(s/us), corticobulbar. 559, 561, 566
- central tegmental, 232–233
- dorsal tegmental, 232
- efferent cochlear, *see* Bundle(s), olivocochlear
- forebrain:
- basal, 451
- lateral, 346, 351, 364, 500, 605
- medial, 234, 346, 351, 364, 457, 460
- mesostriatal, *see* Bundle, nigrostriatal
- nigrostriatal, 233
- olivocochlear, 574
- ventral noradrenergic, 232
- Bushbaby, 531–532, 554, 560
- Butler, A. B., 12, 44, 118–120, 413, 512, 650–652
- Caballero-Bleda, M., 417
- Cadherin, 542
- Caecilians, *see* Gymnophionans
- Caenorhabditis*, 638–639
- Cairney, J., 69
- Calcitonin, 25
- Calcitonin gene related peptide (CGRP), 142, 552, 586
- Callaerts, P., 642
- Calretinin, 418
- Campbell, A. W., 114
- Campbell, C. B. G., 118
- Canal(s):
- central:
- of *Branchiostoma* central nervous system, 648
- of spinal cord, 67, 128–129, 140, 146–147
- lateral line, 33–35
- vertebral, 128, 151
- Canary, 583
- Capsaicin, 188
- Capsule:
- external, 359, 361, 366
- extreme, 359, 361
- internal, 355, 359, 360–361, 364–366, 424–425, 477–478, 619
- otic, 52–53
- Captorhinomorphs, 419, 438–439
- Carassius*, 78, 196, 216, 325, 380
- Carnivora/es, 83, 152, 528, 555, 559
- Carps, 102, 600
- Carr, C. E., 561
- Cartilage:
- hyomandibula(r), 159–160, 195, 200
- mandibular, 159–160
- palatoquadrate, 159–160
- of the throat, 159–160
- Cartilaginous fishes, *see* Chondrichthyans
- Casagrande, V. A., 118
- Catania, K. C., 44
- Catecholamines, *see also* Cell groups, A *and* Dopamine. 277, 293, 295, 301, 303, 626
- Catfishes, *see also* Electric catfishes. 38, 102, 192, 210, 245, 247–249, 251, 305, 397, 453, 499
- Cats, 62, 95–98, 160, 236, 244, 249, 254, 303, 326, 344, 357–358, 384, 479, 505, 526–527, 529–531, 533, 536, 557, 559–560, 578–579
- Cauda equina, 128
- Caudal, term, 61, 665–667
- Cell groups:
- A of Dahlström and Fuxe, 232–233, 268, 293, 300, 303, 396, 473, 478–479, 484
- B of Dahlström and Fuxe, 232–234
- Ch, of Mesulam, 488
- Cell(s), *see also* Neuron(s).
- amacrine, *see* Retina, cells, amacrine
- basket, 246, 253–254, 256–257
- bipolar, *see* Retina, cells, bipolar
- bipyramidal, 513
- bitufted, *see* Cell(s), double pyramidal
- with bottlebrush dendritic endings, 332–333
- Cajal-Retzius, 55–56, 656, 658
- commissural, 140, 143
- Dahlgren, 145
- dorsal, 129, 139–140
- double pyramidal (bitufted), *see also* Cell(s), bipyramidal. 604, 619, 624–625, 630
- edge, *see* Cell(s), marginal
- ependymogial, *see* Cell(s), tanycyte
- eurydendroid, 242, 248–249, 255
- flask-shaped (of *Branchiostoma*), 648
- fusiform, 20, 355
- ganglion, *see* Retina, cells, ganglion
- ganglion(ic), of tectum, 319–321, 330, 332–333
- glial, *see* Glia
- globuli, 639
- Golgi:
- cerebellar, 246, 248–249, 251, 253–254, 256–257
- Type I, *see* Neuron, Golgi, Type I
- Type II, *see* Neuron, Golgi, Type II
- granular, or granule, of:
- cerebellar cortex:
- axons of, *see* Cerebellum, parallel fibers
- dendrites of, 250–253
- general aspects, 246, 249–253, 255–257
- hippocampal formation, 619
- neocortex, 354, 364
- olfactory bulb, 593, 597–598, 600
- visual cortex, 539
- granule-like (of birds), 364
- hair, *see* Receptor, hair cell
- horizontal:
- of medial pallium, 624–625
- of retina, *see* Retina, cells, horizontal
- of tectum, 315–316, 323, 326, 328–329, 334
- infundibular (of *Branchiostoma*), 647–649
- interplexiform, 35–36, 60
- Lugaro, 246, 254
- marginal, of spinal cord, 139, 150
- Mauthner, 20, 141–144, 149, 223, 225–226, 228, 248
- Merkel, 32
- mitral, 593, 595, 597, 600
- Müller, 141, 223, 276
- multipolar, 322–323, 328–329, 334, 624–625
- neuroblasts, 643–644
- periglomerular, 594, 600
- photoreceptive:
- of *Branchiostoma*, 647–648
- of epiphysis, 407–409, 414
- of vertebrates, *see* Retina
- pigment:
- of *Branchiostoma*, 648
- of the skin, 446

- piriform, 20, 23, 312, 315–316, 319–320, 322, 324–326, 328–329, 334
- Purkinje:
- axon, 248–249, 252, 257
 - dendrite, 247–248, 252–253, 256
 - density, 97, 98
 - general aspects, 241, 248, 250–253, 255–257, 262
- Purkinje-like, 247, 256
- pyramidal:
- branched spiny, of teleost tectum, 322, 324–325, 334
 - classification, 20, 23
 - of neocortex, 354, 513
- receptor, *see* Receptors
- Renshaw, 149
- Rohen-Beard, 185
- ruffed, 598
- stellate, 246, 253–254, 256–257, 315, 624
- supramedullary, 140
- tanycyte, 323, 325, 449
- unipolar brush, 246, 254, 258
- X, Y, and W, *see* Retina, cells, P, M, and K
- Center:
- higher vocal (HVC), *see* HVC
 - primary motor (of *Branchiostoma*) (ventral motor neurons), 647, 649
- Central gray, *see* Gray, central
- Central pattern generator, 133, 141, 221, 564, 582, 587
- Centrifugal axons, *see* Axons, centrifugal
- Cephalate, 650–652
- Cephalochordata/es (including *Branchiostoma*), *see also* *Branchiostoma*. 49, 73–74, 638, 644, 646–649, 651–653
- Cepphus*, 217
- Cerebelloid structures, 242, 254, 257–258
- Cerebellum/ar:
- of agnathans, 245–246, 248
 - of amphibians, 242–243, 245–246, 260
 - archicerebellum, 242
 - auricle:
 - general aspects, 241, 245, 247, 250, 276
 - lower leaf, 245, 247, 250
 - upper leaf, 245, 247, 250 - of birds, 242–246, 248, 251, 253–254, 262, 564, 566
 - of cartilaginous fishes, 242–247, 253, 255, 279, 296
 - climbing fibers, 246, 253, 255–257
 - compartmentalization, 255–256
 - corpus, 241, 243–250, 255, 280
 - cortex:
 - afferents, 253–258
 - efferents, 260–262
 - internal connections, 255–257
 - general aspects, 241, 246–258, 261
 - zones of, 255, 261 - crista, 248–249, 257
 - of crossopterygian, 243
 - deep nuclei, 242, 246, 249, 260–262, 273, 284, 290, 300, 322, 429–430, 435–436, 438, 482, 485, 549
 - eminentia:
 - granularis, 246–247, 250, 254, 257, 655
 - ventralis, 246–247 - flocculus, 245
 - folia, 242, 244, 250–251
 - form, 242, 244, 250–251
 - functions, 262
 - general aspects, 52, 64, 67, 69, 109, 131, 133–135, 232, 234, 241–262, 268–269, 271–273, 276–277, 279–281, 312, 317, 344, 351, 356–357, 362–363, 378, 380–381, 385–386, 388, 392–398, 408, 451, 454, 461, 655–658
 - of gymnotids, 245, 259
 - of hagfishes, 243
 - of lampreys, 242–243, 246–247, 256–257, 276
 - layers:
 - granule cell, 241, 243–244, 246–253, 257
 - molecular, 241, 243–244, 246–253, 257
 - Purkinje cell, 241, 244, 246–248, 250, 253–254, 257, 259 - lobes, 243–244, 259
 - of lungfishes, 244, 260
 - of mammals, 242–245, 253–254, 281, 548–549, 555, 559–560
 - of mormyrids, 102, 242–243, 245, 248, 251, 259, 262
 - mossy fibers, 246, 253–257, 388
 - neocerebellum, 242, 245–246
 - of nontetrapods, 246–247
 - nucleus (of gars), *see* Nucleus, cerebellar
 - paleocerebellum, 242
 - parallel fibers, 248, 250, 252–253, 255–256
 - precerebellar nuclei, 242, 256–257
 - of ray-finned fishes, 216, 242–244, 246–248, 253, 255–256, 276, 280, 298
 - of reptiles, 242–243, 245–246, 260, 262
 - size of, 242–243
 - spinocerebellum, 242
 - sulcus, 242
 - of tetrapods, 242, 246, 253
 - valvula, 242, 245–247, 255, 258–259, 262, 276, 280
 - ventricle, 67, 247, 250
 - vermis, 244, 246
 - vestibulocerebellum, 242
 - visuocerebellum, 242
 - weight, 104
 - white matter of, 241, 246
 - zebrins, 255–256
- Cerebral:
- dominance, *see* Hemisphere, specialization
 - hemisphere, *see* Hemisphere, cerebral
 - vesicle, *see* Vesicle, cerebral
- Cerebrum, *see* Hemisphere, cerebral
- Cetaceans, 104–105
- Chaetognaths, 638, 653
- Channel:
- intensity difference, 573–574, 576–577
 - time difference, 573–574, 576–577
- Channel catfishes, *see* Catfishes
- Chemoreceptors, *see* Receptors, gustatory *and* Receptors, olfactory
- Chen, J.-y., 647, 650–652
- Chiasm, optic, 36, 346, 359, 366, 410, 420, 451, 455, 457–459, 500, 524, 527
- Chickens, 105, 448, 574, 254, 257
- Chimaeras, *see* Ratfishes
- Chimpanzees, 83, 95–96, 98, 102, 357–358, 528, 559–560, 581
- Chipmunks, 560, 566
- Chiropterans, *see* Bats
- Chiu, C.-h., 10–11
- Cholecystokinin, 25, 462
- Choline acetyltransferase (CHAT), 471–474, 477, 484, 489
- Chondrichthyans, *see also* Guitarfishes, Skates, Ratfishes, *and* Rays.
- general listing, 41–42, 73–77, 84, 86, 88–89, 95–96, 101–102, 119, 131, 133, 137, 195, 200, 226–227, 344, 350, 399, 407–408, 410, 446, 451, 453, 472, 489, 594–595, 598, 606, 611, 629, 655

- Group I, 86, 88, 275–276, 285, 289–293, 304–305, 316–317, 334, 352, 374, 391–392, 395–396, 410, 418, 420, 432, 472–473, 476, 496, 594, 612, 628, 653–654
- Group II, 88–89, 275–276, 284–285, 290, 292, 295–297, 303, 305, 322–323, 334–335, 354, 375, 378, 392, 395–396, 418, 423, 430, 434, 476, 498–499, 598, 613, 615, 628–629, 653–654
- Chondrocranium, 159–160
- Chondrostei, 76–77, 86–88, 137, 275–276, 281, 304, 317, 375, 496, 499–500, 605, 617
- Chordamesoderm, 51, 643
- Chordata/es, 49, 73–75, 637–638, 643–644, 646
- Chordin, 50, 162
- Choroid plexus, 67
- Chrysemys*, 85, 270, 312, 328, 362
- Cilata*, 38
- Circuits, local, 27, 102, 104
- Cisterna magna, 67
- Clades:
- species-poor, 5
 - species-rich, 5
 - term, 3
- Cladistia (reef-fishes: bichirs and ropefishes), *see also Polypterus*. 76–77, 86–88, 137, 283, 304, 318, 325, 353, 375, 396, 432, 434, 473–474, 477, 496, 499–500, 596, 611, 613, 617, 653–654
- Cladistics/Cladistic analysis, 13–16
- Cladogenesis, 6
- Cladogram(s) (dendrogram), 13, 15, 34, 74, 76–79, 81, 83–85, 96, 137, 303, 505, 527–528, 638, 646
- Clams, *see* Molluscs, bivalves
- Clarius*, 136
- Class, term, 3
- Clastrum, *see also* Formation, clastroamygdalar. 355, 358–360, 366, 502
- Clayton, N., 516
- Clupea*, 186, 379, 423
- Clupeomorpha, *see also Clupea*. 76, 78, 379
- Cnidaria (including hydra and jelly fishes), 638
- Cochlea, 43, 577
- Coelacanth, *see Latimeria*
- Cognition, 104–105, 107–109, 506–507, 514–516
- Coincidence detector, 573–574
- Collateral(s)/Collateralization:
- branch, 27, 140, 143, 223, 574, 600, 657–658
 - recurrent, 143, 149, 248
 - Schaffer's, 620
- Colliculus, *see also* Tectum.
- inferior, 68, 269, 274, 299, 305, 314, 408, 418, 420, 429, 437, 509–510, 577, 579, 581
 - superior, *see* Tectum, optic, of mammals
- Collin, S. P., 118
- Collopallium, *see* Pallium, divisions, collopallium
- Collothalamus, *see* Thalamus, dorsal, divisions, collothalamus
- Columba*, 85, 198, 271, 282, 302, 331, 363, 390–391, 428, 459, 485, 502, 511, 513, 541, 562
- Columella, *see* Bones, columella
- Columnar organization, *see* Organization, columnar and Columns
- Column(s), *see also* Hypercolumns.
- axon, 139, 149
 - branchiomic somatic efferent, 177, 179–180, 186
 - cell, 134, 149
 - Clark's, 150
 - of cortex, *see* Organization, columnar
 - dorsal, 131, 140, 144
 - dorsolateral octaval, 179
 - dorsolateral placodal, 177–179, 191
 - gigantocellular, 222
 - intermediolateral, 148, 179, 152, 462
 - intermediomedial, 148, 462
 - lateral, 140, 144
 - lateralis, *see also* Column, dorsolateral placodal. 195–196
 - magnocellular, 222
 - octaval, 197
 - ocular dominance, 534–535
 - orientation, 534–535
 - parvocellular, 222
 - raphe, 222
 - somatic afferent, *see also* Nucleus, trigeminal, descending. 176–177, 186–193
 - somatic efferent, 176–177, 179–180
 - ventral, 140
 - ventrolateral, of motor neurons, 146–147
 - ventrolateral placodal, 177–178, 191–194
 - ventromedial, of motor neurons, 145
 - vertebral, 128
 - visceral:
 - afferent, *see also* Nucleus, solitarius. 176–177, 193
 - efferent motor, 176–177, 179–180
- Comb jellies, *see* Ctenophora
- Command generator, *see also* Locomotion, rhythmic. 133, 152, 284, 582, 587
- Commissure(s):
- anterior, 359, 361, 364, 366–367, 457, 511, 565, 619
 - anterior pallial, 364
 - habenular, 412
 - hippocampal, 361, 364
 - posterior, 256, 269, 273, 296, 298, 344, 349, 351, 374, 378–379, 388–389, 397, 407, 425
 - tectal, 273–274
- Complex:
- of Böttinger, 589
 - central body, 639
 - clastroamygdalar, *see* Formation, clastroamygdalar
 - forebrain vocal acoustic, 211–212
 - hindbrain vocal acoustic, 211–212
 - inferior olivary, *see* Nucleus, inferior, olivary/olive
 - intralaminar, midline, and mediodorsal (IMMC) (of mammals), 437
 - lateral mesencephalic nuclear, *see* Nucleus, lateral(is), mesencephalic, nuclear complex
 - lateral posterior/pulvinar, *see* Nucleus, lateral(is), posterior/pulvinar complex
 - medialis, *see* Nucleus, medial(is), complex
 - midbrain vocal acoustic, 211–212
 - oculomotor, *see* Nucleus, oculomotor
 - opticus principalis thalami (OPT), of birds, *see* Nucleus, dorsal(is), lateral geniculate, of birds
 - parabrachial, 457
 - pineal/parapineal, *see* Pineal/parapineal complex
 - preglomerular, *see* Preglomerular nuclear complex
 - striatopallidal, *see* Striatopallidal complex(es)
 - subpretectal (of birds), *see* Nucleus, subpretectalis and Nucleus, interstitio-pretectalis-subpretectalis
 - supragenulate/limitans, *see* Nucleus, supragenulate/limitans
 - ventrobasal/ventrolateral, *see* Nuclear group (of dorsal thalamus of mammals), ventral
- Complexity, *see* Evolution, of complexity
- Condylura*, 33, 328

- Cone(s), *see also* Receptors, light.
 growth, 57
 of retina, 31, 35
- Conjunction, 15
- Conodonts, 75, 644, 646, 650
- Consciousness, 30, 107–108, 506–507
- Contralateral, term, 666
- Convergence/Convergent evolution, 9, 13, 617
- Cope, E. D., 116
- Cord, nerve:
 dorsal/dorsal hollow, 645, 647, 651
 general aspects, 641
 ventral, 645
 spinal, *see* Spinal cord
- Cornea, 217, 652
- Cornu Ammonis, *see* Hippocampus, Ammon's horn
- Coronal, term, 666
- Corpus:
 callosum, 355, 357, 359, 361, 364, 366, 511, 532, 621, 623, 656
 geniculatum thalamicum (of frogs), *see* Nucleus, corpus geniculatum thalamicum
 Luysii, *see* Nucleus, subthalamic, of mammals
 striatum, *see* Striatopallidal complexes
- Corpuscle:
 Meissner's, 31–32
 Pacinian, 31–32
 encapsulated, 33
- Cortex, *see also* Pallium.
 auditory:
 areas:
 A1, 502, 504, 509, 577–579, 586–587
 A2, 577–579
 belt, 577, 579
 general aspects, 105, 234, 357, 420, 429, 577–579, 581, 588
 blobs, 534–535
 calcarine, *see* Cortex, visual, areas, V1 (striate)
 cerebellar, *see* Cerebellum, cortex
 cingulate:
 anterior, 587–588
 general aspects, 429–430, 435, 551
 columnar organization, *see* Organization, columnar
 convolutions, 106
 development, 55–57, 356
 dorsal (of reptiles), 343, 361–362, 436, 456, 488, 502, 504, 507–508, 510–511, 535, 539–541, 560–564, 580, 623–626, 629
 dorsolateral (of reptiles), *see* Cortex, dorsal (of reptiles)
 dorsomedial (of reptiles), 361–362, 502, 562, 564, 580, 623–626, 629
 entorhinal, 358, 503–504, 618–623, 626, 628–630
 extrastriate, *see* Cortex, visual, extrastriate
 general aspects, 353–358, 361–365
 frontal, 549, 551–552
 general aspects, 232–233, 236
 granular:
 term, 355
 of visual cortex, 539
 gyrencephalic, *see* Gyrencephaly
 inferotemporal, 535
 insular:
 general aspects, 357, 359, 503, 551–552, 557
 dysgranular area, 557
 granular area, 557
 interblobs, 534–535
 koniocortex, term, 355
 lateral, 60, 362, 436, 497–498, 502, 539–540, 562, 564, 580, 601–602, 604, 625
 layers of neocortex:
 I (1) (molecular), 56–57, 354–355, 531
 II (2) (external granular), 56–57, 119–120, 354–355, 364, 510–511, 530–531, 534–535, 656
 III (3) (external pyramidal), 56–57, 119–120, 354–355, 364, 511, 530–531, 534–535, 656
 IV (4) (internal granular), 56–58, 119–120, 354–355, 364, 510–511, 534, 555, 656
 4A, 535
 4B, 535
 4Ba, 530–531, 534–535
 4Bβ, 530–531, 534–535
 V (5) (internal pyramidal), 56–57, 119, 355, 363, 531
 VI (6) (multiform), 56–57, 119, 355, 363, 531
 general aspects, 56–57
 infragranular (V and VI), 355, 363
 limbic, 233, 558
 lissencephalic, *see* Lissencephaly
 medial, 361–362, 436, 502, 539, 562, 564, 580, 604, 623–626, 629
 motor:
 areas:
 M1, 502–503, 558–560, 581, 589
 M2, 558–560, 587
 M3, 558
 general aspects, 105, 261, 357, 429, 557–559, 561, 566, 589
 primary, 429, 558
 supplementary, 502–503, 558, 587, 588
 olfactory, *see also* Cortex, lateral. 60, 353, 355, 357–358, 360, 363, 366, 430, 435, 438, 482, 502–503, 510–513, 593, 597, 600–602, 605, 619
 orbitofrontal, 619
 parasubicular, 619–620
 parietal:
 general aspects, 356–357
 posterior, 502–504, 506, 535, 549–551, 557
 patches, *see* Cortex, blobs
 perirhinal, 549, 551
 piriform, *see* Cortex, olfactory
 posterior insular, 548–550, 556
 prefrontal, 357, 430, 435, 438, 482, 487, 502–504, 506–507, 510, 514, 588, 600, 611
 premotor, 357, 502–503, 558–560
 presubicular, 619–620
 puffs, *see* Cortex, blobs
 radial organization, development of, 54–57
 retroinsular, 537, 557
 somatosensory/sensorimotor:
 areas:
 S1, 429, 436, 502–505, 507–508, 548–552, 554–557, 559, 561
 S2, 429, 504, 508–509, 548–552, 554, 556–557, 561
 S3, 557
 S4, 549, 551, 557
 S5, 557
 general aspects, 45–46, 94, 357, 548–549, 552, 554, 556, 558, 656–657
 striate, *see* Cortex, visual, V1 (striate)
 subicular, 357–358, 361, 618–623, 626–630
 sulcus, *see* Sulcus/i
 term, 26, 55
 thickness of, 105–106

- transitional, 353, 361
- ventral cell plate(of snakes), *see* Plate, ventral cell (of snakes)
- visual:
 - areas:
 - extrastriate, 429–430, 502, 504–505, 508–509, 532–533, 530, 543
 - general aspects, 351, 357, 380, 385–386, 393
 - middle temporal (MT), 532–534, 536, 543
 - V1 (striate), 357, 429, 435, 501, 504–505, 507–509, 530–532, 535–538, 558, 578
 - V2, 531, 534–535
 - V3, 532, 534–535
 - V4, 532, 534–535
 - V5, 532
 - general aspects, 105, 531, 542, 533, 535–536, 577
 - volume, *see* Brain, size
- Cortical recruiting response, 436
- Corticostatin, 235
- Corticotropin, *see* Adrenocorticotrophic hormone
- Corticotropin releasing hormone, 25
- Cows, 105, 303, 560
- Craigie, E. H., 69
- Craniates, term, *see also* Vertebrates. 73, 75
- Crocodyles, 33–34, 79–81, 86, 89, 96, 119, 145–146, 184, 208, 226, 243–244, 248, 251, 283, 301, 303, 352, 362, 387–389, 409, 414, 436, 576, 603, 606, 627–628
- Cromwell, O., 109
- Crosby, E. C., 69, 113, 115
- Crossopterygian, term, *see also* Latimeria. 76
- Crows (corvids), 514, 516, 628
- Crus cerebri, term, 289
- Crustacea/ns, 638, 641
- Cryptomys*, 313
- Csillag, A., 514
- Ctenophora (comb jellies), 638
- Cup, *see* Arcopallium, cup
- Curwen, A. O., 69
- Cuvier, G., 69, 641
- Cyclic AMP, 25
- Cyclic GMP, 25
- Cyclostomes, *see* Agnathans, Hagfishes, *and* Lampreys
- Cynodont, 525
- Cyprinus*, 197
- Cytochrome oxidase, 534
- Dahlström, A., 293
- Danio* (zebrafish), 413, 605, 615
- Darkschewitsch, L.O., 69
- Darwin, C., 3, 5–6, 8, 113
- Deacon, T. W., 117
- deBeer, G., 12
- Decussation:
 - of corticospinal tract, 151
 - of optic nerve, *see* Chiasm, optic
 - supraoptic, 351, 426–427, 458, 461
 - term, 547
- Deer, 560
- Degeneration:
 - anterograde, 27, 29
 - retrograde, 27, 29
- Delamination, 643–644
- DeLange, S. J., 69
- Delay line, 574
- den Boer-Vissen, A. M., 344
- Dendrites:
 - apical, 23, 354
 - basal, 23
 - branches, 20
 - classification, 21–23
 - general aspects, 20–23, 223
 - organization, *see* Organization, dendritic
- Dendrogram, *see* Cladogram
- de No, L., 357
- Depolarization, 25
- Dermatocranium, *see* Bones, dermal
- Dermopterans, 528
- De Robertis, E. M., 641
- Deuterostomes, 49, 637–638, 641, 644–646
- Deutocerebrum, 639–641, 645
- Development (embryological):
 - of invertebrate central nervous system, 639–643
 - of vertebrate central nervous system, general aspects, *see also* listings under individual topics. 49–61
- Diacycloglycerol, 25
- Diamond, I. T., 116–118
- Diapsid(s), term, 80–82, 86, 96, 656
- Diencephalon:
 - general organization, *see also* Epithalamus, Hypothalamus, Pretectum, Thalamus, *and* Tuberculum, posterior. 50, 52, 164, 312, 343–347, 349–352, 357, 362, 645, 648–649, 651–653, 655, 658
 - weight, 104
- Dimorphism, sexual, *see* Sexual dimorphism
- Dinosaurs, brain size, 103
- Dipnoi, *see* Lungfishes
- Discs, Merkel's, 31, 33
- Distal, term, 666
- Divac, I., 514
- Diversity, biological, 4
- Dobzhansky, T., 3
- Dogs, 105, 559–560, 566
- Dolphins, 98, 572–573
- Domestication, 105
- Dominance:
 - cerebral, *see* Hemisphere, specialization
 - hemispheric, *see* Hemisphere, specialization
- Donoghue, P. C. J., 644
- Dopamine (DA), *see also* Catecholamines *and* Cell groups, A. 25, 142, 273, 289, 293–297, 300, 396, 438, 471–474, 476–479, 483–485, 487–488, 502, 504, 510, 514, 586, 605, 623, 629
- Doppler shift, 578
- Doré, J.-C., 104
- Dorsal:
 - term, 61, 666–667
 - ventricular ridge:
 - anterior part, *see also* Arcopallium, Entopallium, *and* Nidopallium, area L pallii. 119–120, 333, 361–362, 432, 484, 502, 504, 507, 509, 511, 540, 562–564, 580, 656–657
 - general aspects, 59–60, 70, 119, 305, 343, 363, 426, 431–432, 465, 488, 495, 504, 508–510, 513, 539, 564, 576, 579–581, 601, 603, 657–658
 - posterior part, *see also* Amygdala, nucleus, external (of reptiles); Amygdala, nucleus, posterior (of reptiles); Amygdala, nucleus, posterioris amygdalopallii (PoA) (of birds); Amygdala, nucleus, sphericus (of squamates); Amygdala,

- nucleus, taeniae amygdalae (TnA) (of birds); *and* Amygdala, nucleus, ventral anterior (of reptiles). 504, 511
- proto-DVR, 120
- Dreaming, 223, 236
- Drosophila* (fruit fly), 54, 162, 637–643
- Dubbeldam, J. L., 344
- Ducks, 152, 211, 230
- Dugas-Ford, J., 510
- Dura mater, *see* Mater, dura
- Durward, A., 69
- Dynein, 21
- Dyslexia, 95
- Eagles, 540
- Ebbesson, S. O. E., 117–119, 121, 485, 657
- Ebner, F. F., 118–119
- Ecdysozoa, 638–639
- Echidnas, 41, 83–84, 151–152, 205, 235, 357, 504, 559–560, 554–555
- Echinodermata/s, 49, 638, 644, 646
- Echolocation, 305–306, 572, 578
- Ectoderm, 49, 51, 643–644, 657
- Ectoatriatum:
- belt, *see* Perientopallium
 - core, *see* Entopallium
- Edinger, L., 69
- Edinger, T., 69
- Edwards, C., 575
- Eels, *see also* Electric, eels. 281
- Eigenmannia*, 197, 397, 616
- Eimer, G. H., 117
- Eimer's organs, *see* Receptors, mechanosensory, Eimer's organs
- Elaborated, term, *see also* Group II, term. 85
- Elasmobranchs/i, term, *see also* Sharks, Skates, *and* Rays. 76, 86
- Eldredge, N., 3, 6
- Electric:
- catfishes, 41, 144
 - fishes, 41, 144, 259–260
 - eels, 41, 144
 - field, *see* Field(s), electric
 - organ, *see* Organ(s), electric
- Electroencephalogram (EEG), 234–235
- Elephants, 98, 249, 559–560
- Elliott Smith, G., 69
- Elopomorpha, 76, 78, 290
- Elops*, 186
- Elston, G., 560
- Eminence, median, 233, 446–448, 460
- Eminentia:
- granularis, *see* Cerebellum, eminentia granularis
 - medialis, *see* Eminence, median
 - ventralis, *see* Cerebellum, eminentia ventralis
- Endocrine system, 446, 551
- Endoderm, 49, 51–52, 161
- Endopiriform nucleus/formation, *see* Nucleus, endopiriform *and* Formation, claustrum-endopiriform
- Enkephalin (ENK), 462, 471–474, 476–478, 480, 482–487, 489
- Enlargement:
- cervical, 145–147, 151
 - lumbar, 145–147, 151
- Enteropneusta/s, *see* Hemichordata/es
- Entopallium, 330, 333, 347, 363, 431, 502, 509, 540–541, 543, 565, 580
- Epidermis, 52, 55
- Epimere, 52, 159, 161–162
- Epinephrine, 24–25, 232
- Epiphyseal stalk, 66
- Epiphysis, *see also* Pineal (eye/gland/organ). 52, 66, 407–409, 414, 449–451, 453, 651
- Epithalamus:
- of amphibians, 407–410, 414
 - of birds, 407, 409, 412
 - of cartilaginous fishes, 407–408, 410
 - general aspects, 65–66, 180, 343, 345, 379, 407–414, 611, 622
 - of hagfishes, 407, 410, 414
 - of lampreys, 407–408, 410, 414
 - of mammals, 407–410
 - of ray-finned fishes, 407–408, 410, 413–414
 - of reptiles, 407, 409, 412, 414
- Epithelium:
- gustatory, 38
 - olfactory, 39, 594–595, 603
 - pigment, 35–36
- Eptatretus*, 74–75, 279, 295, 321, 354, 410, 422, 476, 498, 615
- Eryx*, 625
- Esox*, 380, 382–383
- Estrogen, 450
- Eugerres*, 324–325
- Eulipotyphla/ns, 33, 83, 104, 114, 355, 526, 531, 553, 556, 559, 566
- Eusthenopteron*, 137
- Euteleostei, term, *see also* Actinopterygians, teleosts (including Euteleostei). 76, 78
- Eutheria, term, *see also* listings for individual eutherian mammals. 80, 86
- Evagination, of telencephalon, 58, 135, 595
- Eversion, of telencephalon, 58–59, 495–497, 499, 595, 616
- Evo-devo, term, 7, 642
- Evolution/ary:
- of accessory optic system, 395–396
 - of auditory system, 213–214, 588–589
 - of brain in vertebrates:
 - early vertebrates, general aspects, 649–657
 - mechanisms, 657–659
 - of cerebellum, 243, 245–246, 262
 - and/of complexity, 96–97
 - of cranial nerves (of the hindbrain and midbrain), 290, 649–655
 - Darwin-Wallace theory of, 113
 - of dorsal pallium (of amniotes), 361–364, 512
 - of dorsal thalamus, 399, 417–419, 432–434, 437–439
 - of electroreception, 188, 195, 197, 397–398
 - of epithalamus, 414
 - general features, 99,
 - of glia, *see* Glia, evolution
 - of heart, 99,
 - of hindbrain, 136–138
 - of hypothalamus, 462–463
 - innovation, 10
 - of intelligence, 107
 - of interpeduncular nucleus, 285
 - of isthmo-optic nucleus, 284
 - of lateral line system, 194–197
 - of limbic system, 629–630
 - of locus coeruleus, 278, 281
 - mechanisms:
 - changes in:

- homeobox gene patterning, 658
- neuronal migration, 658–659
- neuronal proliferation, 658–659
- radial organization, 658–659
- differentiation of multiple areas/groups of neurons, 58–659
- duplication of areas/groups of neurons, 658–659
- gain of:
 - connections, *see* Evolution/ary, mechanisms, invasion
 - new cell phenotypes, 658–659
- induction, 657–658
- invasion, 658
- loss of connections per se, 658
- parcellation, 658
- of mesencephalic nucleus of trigeminal nerve, 290
- of midbrain locomotor region, 285
- of motor system, 205–218, 566–567, 654–655
- of nucleus basalis (cholinergic cell group), 489
- of nucleus isthmi, 283
- of olfactory system, 606
- of optic tectum, 334–335
- of pain pathways, 553
- phyletic (anagenesis), 97–99
- of posterior tuberculum, 303, 399
- of pretectum, 394–396
- progress, 4, 97–99
- of raphe nuclei and ascending serotonin system, 277
- of red nucleus, 292
- of reticular formation, 236
- selective pressures/advantage, 5, 7, 98, 100, 102, 104–106
- of sensory systems, general aspects, 46–47, 183–200
- of skull, 81–82, 649, 651
- of somatosensory system, 566–567
- of spinal cord, 152
- of striatopallidal complexes, 489
- of substantia nigra and ventral tegmental area, 303
- of terminal nerve, 606
- of torus lateralis, 304
- of torus longitudinalis, 257–258, 319, 325
- of torus semicircularis, 306
- of visual system, 540–543
- of vocal pathways, 588–589
- of vomeronasal system, 606
- Evolutionary synthesis, 3
- Excitation, feed forward, 254
- Extinction:
 - general aspects, 4, 100
 - mass, 4–5
- Eye(s), *see also* Retina.
 - cyclopic, 650
 - development (anlagen), 53–53, 641–642, 650
 - epiphyseal/median (parapineal, parietal, pineal), 36–37, 345–346, 407–409, 413–414
 - evolution of, general aspects, 641–642
 - frontal (of *Branchiostoma*), *see* Organ, frontal (of *Branchiostoma*)
 - median, *see* Eye, epiphyseal
 - movements, 242, 558
 - ocelli/us, 641–642, 645, 647
 - ommatidia/l, 641–642
 - paired/lateral (evolution and development of), 641, 645, 649–652, 654, 657
 - parapineal, *see* Eye, epiphyseal
 - parietal, *see* Eye, epiphyseal
 - pigment cup, 641
 - pineal, *see* Eye, epiphyseal
 - preoptic/hypothalamic (in *eyeless* mutation), 651
 - retinal type (evolution of), 641–642, 647
 - sclera, 217
 - spots, 642
 - stalk, 650
- Face, somatosensory representation of, *see also* Snout. 550, 561
- Family, term, 3
- Fasciculus/i:
 - arcuate, 587–588
 - cuneatus, 150
 - dorsal longitudinal, 460
 - gracilis, 150
 - lenticular (field H₂ of Forel), 478
 - medial longitudinal, 216, 218, 227, 230, 249, 269, 271–273, 276, 279–281, 291–298, 301, 391–392
 - retroflexus, 269, 272–273, 285, 291–292, 296–298, 346, 349, 373–374, 376–379, 392, 397, 408, 410–414, 420
 - subthalamic, 478
 - thalamic (field H₁ of Forel), 478–479
 - uncinate, 261–262
- Feathers, 31
- Felis*, 384
- Fenestra, of skull, 80–82, 524–525
- Ferret, 527, 529
- Fiber(s):
 - axonal, *see* Axons
 - centrifugal, *see also* Bundle(s), olivocochlear. 600
 - climbing, *see* Cerebellum, climbing fibers
 - mossy:
 - of cerebellum, *see* Cerebellum, mossy fibers
 - of hippocampal formation, 620
 - parallel, *see* Cerebellum, parallel fibers
 - Reissner's, 145, 648–649
 - woolly, 472–474, 484
- Field(s):
 - barrel, *see* Barrels, somatosensory
 - binocular, *see* Vision, binocular
 - CA1–CA4 of hippocampal formation, *see* Hippocampus, CA1–CA4 fields
 - developmental, *see* Field(s), morphogenetic
 - electric, 21, 41–42, 259
 - embryonic, *see* Field(s), morphogenetic
 - frontal eye, 357, 499, 549, 551, 558
 - H of Forel, *see* Nucleus, reticular(is), subthalamic
 - H₁ of Forel, *see* Fasciculus, thalamic
 - H₂ of Forel, *see* Fasciculus, lenticular
 - homology, *see* Homology, field
 - L (of birds) *see* Nidopallium, area L pallii
 - morphogenetic, 6–7, 9–12, 57, 438
 - posterodorsal tegmental (of anurans), 278
 - posteroventral tegmental (of anurans), 278
 - receptive, 46, 530
 - retrobulbar (A8), 478, 484
 - visual, *see* Visual, field
- Fimbria, *see* Tract, fimbria
- Fin, pectoral, 137
- Finches, 152, 583, 586
- Finger, T. E., 38
- Fishes:
 - cartilaginous, *see* Chondrichthyans
 - general aspects, 32, 73–78, 593
 - electric, *see* Electric, fishes
 - fleshy-finned, *see* Sarcopterygians
 - jawless, *see* Agnathans
 - ray-finned, *see* Actinopterygians

- rhypidistian, 136–137
- sonic, 420
- teleost, *see* Actinopterygians, teleosts
- Fishunculi, 499, 501
- Fissure, term, *see also* Sulcus/i. 66
- Flatworms, *see also* *Planaria*. 639
- Flavor, 38
- Flechsig, P., 114
- Floor plate, *see* Plate, floor
- Fluid, cerebrospinal, 67, 146, 449
- Fly, *see* *Drosophila*
- Foramen/ina, of:
 - Lushka, 67
 - Magendie, 67
 - Monroe, interventricular of, 67
- Forebrain (Prosencephalon), *see also* Diencephalon and Telencephalon.
 - basal, 232, 364–369, 471–489, 600
 - collothalamic, *see* Pallium, divisions, collopallium and Thalamus, dorsal, divisions, collothalamus
 - general aspects, 50, 52–53, 65, 168, 343–369, 640–641, 646, 649, 653, 655
 - lemnthalamic, *see* Pallium, divisions, lemnopallium and Thalamus, dorsal, divisions, lemnothalamus
- Forel, A., 478
- Forelimb:
 - evolution, 137–138
 - general aspects, 43
- Forepaw:
 - evolution, 100, 137
 - general aspects, 557
 - somatosensory representation of, 43–45
- Forey, P. L., 644
- Formation:
 - claustroramygdalar, 59–60, 120, 359–360
 - claustrum-endopiriform, 343, 360–361, 504, 511
 - hippocampal, *see* Hippocampus
 - reticular, *see* Reticular formation
- Fornix, *see* Tract, fornix
- Fossa, interpeduncular, 272
- Foster, R. E., 119
- Fovea, 529
- Foxes, 98, 249, 523, 537
- France, A., 109
- Frederikse, A., 69
- Freud, S., 129, 185
- Fritsch, G., 605
- Frogs, *see* Anurans
- Frontal, term, 666
- Frost, B., 542
- Fruit fly, *see* *Drosophila*
- Funiculus/i:
 - general aspects, 129
 - lateral, 232
 - ventral, 232
- Furlong, R. F., 75
- Fuster, J. M., 506–507, 514
- Fuxe, K., 293
- Gage, S. P., 69
- Gambusia*, 413
- Gamma-aminobutyric acid (GABA), 25, 142, 150, 230, 232–233, 235, 248, 253–254, 273, 283, 292, 296, 300, 352, 365, 387, 393–394, 471–474, 476–487, 552, 626
- Gamma efferents, 129
- Ganglia/on:
 - basal, term, *see also* Striatopallidal complex(es). 66, 471
 - ciliary, 206, 215, 217, 375
 - cranial nerve, 135, 184
 - dorsal root, 129, 132–133
 - Gasserian, 135
 - hypocerebral, 639, 645
 - otic, 206
 - parasympathetic, *see also* Autonomic nervous system. 134, 148, 462
 - prothoracic, 639, 645
 - pterygopalatine, 206
 - Scarpa's, 135
 - semilunar, 135
 - sensory, 21, 31
 - spiral, 135
 - subesophageal, 639–641, 644–645
 - submandibular, 206
 - sympathetic, *see also* Autonomic nervous system.
 - chain of, 462
 - general aspects, 129, 132, 134, 148, 462
 - trigeminal, 135
- Gans, C., 164, 649, 652
- Garengot, R. J. C., de, 618
- Gars, *see* Ginglymodi
- Gastropoda/s, 639
- Gastrula, 49, 638
- Gastrulation, 49, 51, 159, 647
- Gehring, W. J., 642
- Gekko*, 362, 564
- Gene products:
 - bone morphogenetic proteins (BMPs), 643–644, 657
 - chordin, 643–644, 649, 657
 - decapentaplegic (dpp), 643–644, 657
 - short gastrulation (sog), 643–644, 657
 - Sonic hedgehog (Shh), 50, 54–55, 650
- Gene(s):
 - alleles, 5–6
 - altruism, 6
 - AmphiEuxA* (of amphioxus, i.e., *Branchiostoma*), 653
 - brachyury*, 644
 - decapentaplegic* (dpp), 643
 - empty spiracles* (ems/Emx), 640–641
 - engrailed* family genes, 53
 - Eux* family genes, 653
 - fitness, 5
 - flow, 5
 - forkhead* (*fh/HNF-3β*), 640
 - goosecoid*, 644
 - homeobox, general aspects, 53–54, 162, 657–658
 - Hox* (homeobox) family genes:
 - AmphiHox3* (of amphioxus, i.e., *Branchiostoma*), 649
 - general aspects, 53–54, 640–641, 646
 - Hox3*, 648–649
 - HrHox-1* (of ascidian), 646
 - Hroth* (of ascidian), 646
 - isolating mechanisms, 5
 - Krox* (zinc-finger) family genes, 53–54
 - LIM-homeodomain, 612, 630
 - Math4a*, 418
 - orthodenticle* (*otd/Otx*), 640–641, 646
 - Pax* (paired box) family genes:
 - general aspects, 54, 646
 - HrPax-258* (of ascidian), 646
 - Pax6* (*eyeless*, *Small eye*, *Aniridia*), 640–642, 650–651
 - pleiotropic, 6

- recombination, 5
- short gastrulation (sog)*, 643
- Sonic hedgehog (Shh)*, 650–652
- tailless (Tll/Tlx)*, 640–641
- Wnt* family genes, 53–54
- Gennari, F., 531
- Gennari, line (stripe) of, 531
- Genus, term, 3
- Geoffroy Saint-Hilaire, E., 641, 644
- Gerbils, 578
- Geschwind, N., 114
- Ghiselin, M. T., 8
- Ghrelin, 448
- Gibbons, 528
- Gilbert, S., 7
- Gilland, E., 166
- Gills, 158–159, 170
- Ginglymodi (gars), 64–65, 76–78, 87–88, 275–276, 281, 283, 292, 304–305, 318, 344, 375, 396, 413, 453, 497
- Ginglymostoma*, 354, 498
- Giraffes, 27, 128
- Gisi, M. J., 69
- Gland(s):
 - adrenal:
 - cortex, 447
 - medulla, 463
 - general aspects, 20, 445
 - lacrimal (tear), 206, 463
 - pineal, *see* Pineal (eye/gland/organ)
 - sweat, 463
 - salivary, 206, 211, 463
- Glia/l:
 - evolution, 89
 - fibrillary acidic protein (GFAP), 89
 - radial, 54–55
 - Schwann cells, 162
- Globus pallidus, *see* Nucleus, globus pallidus
- Glomerulus:
 - cerebellar, 251–254
 - olfactory, *see* Olfactory, glomerulus
- Glucagon, 25, 461
- Glucose, 461, 463
- Glutamate/glutamatergic, 25, 142, 158, 235, 478–479, 481–487, 552
- Glutamic acid decarboxylase (GAD), 255
- Glycine, 25, 142, 150, 254
- Gnathonemus*, 397
- Gnathostomes, 73–74, 86, 644, 646, 653, 655
- Goats, 357–358, 560
- Goldby, E., 69
- Goldfishes, *see also* *Carassius*, 39, 78, 95–96, 192, 194, 196, 216, 228, 244, 247, 325, 380, 392, 398–399, 410, 430, 448, 499, 501, 616–617, 629
- Golgi, C., 69
- Gonadotropin-releasing hormone (GnRH), *see* Hormone, gonadotropin-releasing (GnRH)
- Gorillas, 102, 528
- Gould, S. J., 6
- Grades, 99
- Gray:
 - central, 227, 269, 279, 281, 295, 299, 311, 321, 325–326, 424–425
 - isthmal, 270, 276
 - periaqueductal, 212, 314, 325, 384, 460, 487, 551, 553, 587–589
 - periventricular, 294, 298
 - pretectal (of anurans), 375, 377
 - rhombencephalic central, 276
 - spinal, *see* Spinal cord, gray matter
 - tectal:
 - of birds, 387, 390
 - of turtles, 386
 - tegmental central, 321
- Greek, roots of anatomical terms, 668–670
- Gregory, J. E., 188
- Ground squirrels, 326
- Group I, term, 57, 85–89, 267
- Group II, term, 57, 85, 87–89
- Growth:
 - of body, *see* Body, growth
 - cone, *see* Cone(s), growth
 - hormone, 25–26, 447–449, 453
 - hormone-releasing hormone, 25
- Guillén, M., 417
- Guinea pigs, 251, 554
- Guitarfishes, 277, 453
- Gulls, 138
- Güntürkün, O., 514, 542
- Gymnophionans, 78–79, 304
- Gymnotiformes, 212–213, 298, 305, 499, 501
- Gyrencephalic/y, 66, 356
- Gyrus/i:
 - cingulate, 357–359, 618, 620–623
 - dentate, 355, 357, 361, 618–620, 622–623, 626–630
 - development, 356
 - parahippocampal, 618
 - term, 66, 356
- Habenula:
 - of amphibians, 410, 433
 - of birds, 302, 412, 459
 - of cartilaginous fishes, 420
 - general aspects, 66, 233, 268–269, 345, 373, 384, 409–414, 451, 482–483, 613, 653
 - of hagfishes, 354, 410, 422, 498, 615
 - of lampreys, 410, 612
 - of lungfish, 456
 - of mammals:
 - anterior paraventricular nucleus, 411–412
 - general aspects, 355, 411–412, 622, 629
 - lateral nucleus, 411, 424–425
 - medial nucleus, 411, 424–425
 - posterior paraventricular nucleus, 411–412
 - of ray-finned fishes, 350, 421
 - of reptiles, 351, 412–414, 629
- Habitat:
 - fragmentation, 4
 - generalists, 4
 - specialists, 4
- Hagfishes, 74–75, 86–88, 96, 188, 197, 214, 275, 279, 283, 285, 294–295, 321, 334, 353–354, 375, 392, 396, 407, 410, 414, 417–418, 422, 434, 453, 472, 476, 489, 498, 595, 597–598, 606, 613, 615, 628, 646, 652–654
- Haikouella*, 74, 646–647, 649–653
- Halder, G., 642
- Halecomorphi, *see* *Amia*
- Hall, W. C., 116–119
- Halocynthia*, 646
- Halpern, M., 604
- Hamsters, 488, 560, 566
- Hand, 137

- Harting, J. K., 118
Hartline, P., 187
Hawks, 540
Head:
 general aspects, 134, 158–170
 segmental organization, 158–179
Heart:
 evolution of, *see* Evolution, of heart
 rate, 233, 455, 463
Hedgehogs, 33, 98, 105, 151, 355, 555, 560, 578
Hedges, S. B., 82
Heimer, L., 118
Hemichordata/es (Enteropneusta/s, including acorn worms), 49, 638, 644–646
Hemisphere:
 animal, 49, 51
 cerebral, 66
 specialization, 587
 vegetal, 49, 51
Hennig, W., 9
Herkenham, M., 26
Herrick, C. J., 69, 113, 115–117, 343
Herrick, C. L., 69
Heterochrony, 6, 61
Heterodontus, 227
Higher vocal center, *see* HVC
Hindbrain (Rhombencephalon):
 embryology, 135
 general aspects, 50, 53, 64–65, 67, 69, 104, 133–136, 312, 344, 356, 641, 645–647, 649, 651–655, 658
 medulla, 64–65, 133, 176–180, 244, 357
 pons, 64, 133, 135, 177, 357
Hind limb, 43
Hines, M., 69
Hippocampus/hippocampal formation:
 Ammon's horn (Cornu Ammonis), 355, 357, 361, 618–619, 621–623, 626–630
 of birds:
 dorsolateral, 626, 628
 dorsomedial, 626–628
 general aspects, 348, 502, 511, 513, 626–630
 nomenclature, 348
 parahippocampal area, 348, 513, 626
 V-shaped, 626, 628
 CA1–CA4 fields, 355, 357, 504, 619–622
 dentate gyrus, *see* Gyrus, dentate
 development, 621
 general aspects, 60, 66, 232, 234, 300, 355, 357–358, 369, 411, 450, 455, 457, 460, 488, 565, 600, 611, 618, 641
 of goldfish, 499, 501, 611, 615–617, 629–630
 of mammals, 499, 502, 504, 510, 618–623, 628–630
 pallium, 353, 619
 of reptiles, 502, 623–626, 629–630
 terminology, of mammals, 618
Hirth, F., 541
Histamine, 25, 235
His, W., 69
Ho, M.-W., 14
Hodos, W., 44, 118
Hofman, M. A., 104, 106
Holland, N. D., 647
Holland, P. W., 75, 649
Holmgren, N., 69
Holobranch, *see* Head, segmental organization
Holocentrus, 500
Holocephali, term, *see also* Ratfishes, 76, 86
Holosteans, 244, 248, 257
Homeobox, *see* Genes, homeobox
Homo (human), 83–84, 95–98, 105, 137–138, 148, 249–250, 356–357, 478, 501, 503, 506–507, 514, 527, 559–560, 581, 587, 589, 619, 621, 623, 629
Homogeny, term, 9
Homology:
 biological, 11–12
 criteria/tests, 15
 discrete (one-to-one/specific/strict), 9, 657
 field, 9–11, 120, 438, 511, 527, 543, 580, 626, 630, 657
 general aspects, 8–13, 15, 543
 generative (syngeny), 12–13, 15, 407, 413, 495, 617, 658
 historical, 8, 11–13, 15, 495
 iterative (serial), 9, 164
 latent, 12
 minuteness of resemblance, 9
 multiplicity of similarity, 9
 one-to-one, *see* Homology, discrete
 phyletic, 8
 serial, *see* Homology, iterative
 specific, *see* Homology, discrete
 specification, 8
 strict, *see* Homology, discrete
Homonymy, 9
Homoplasy, 9, 11, 13, 116
Homunculi, 499
Horizontal, term, 667
Hormone:
 androgens, 450, 457
 anterior pituitary, 25–26, 447–449, 453, 455
 estrogens, 450
 gonadotropin-releasing (GnRH) (leuteinizing hormone-releasing, LHRH), 25, 163, 168, 181, 408–409, 605, 652
 growth, *see* Growth, hormone
 hypophyseal, hypothalamic, 25–26, 447–449
 hypothalamic:
 inhibiting, 447, 449
 releasing, 25, 447, 449, 453
 leuteinizing, 25, 41
 leuteinizing hormone-releasing (LHRH), *see* Hormone, gonadotropin-releasing
 melanocyte stimulating (MSH), 447–449, 453, 455
 neurotransmitter, 25
 posterior pituitary, 25–26, 447, 460
 testosterone, 151
 thyroid stimulating hormone (TSH), 25, 447
 thyrotropin-releasing hormone (TRH), 25, 453
 trophic, 26, 461
Horn, *see* Spinal cord, dorsal horn *and* Spinal cord, ventral horn
Horses, 98, 105, 137, 249–250
Hubel, D., 533
Huber, G. C., 69, 115
Human, *see* *Homo*
Humphrey, O. D., 69
Huntington's disease, 296, 303
Huxley, J., 3–4
HVC:
 general aspects, 347, 584–587
 shelf, 585, 587
Hydra, *see* Cnidaria
Hydrolagus, 75, 77
5-Hydroxytryptamine, *see* Serotonin
Hyla, 586

- Hypercolumns, 531, 535, 577
- Hyperpallium (H), *see also* Wulst.
- apicale (HA), 346, 363, 502, 511–512, 541, 560, 562, 565
 - densocellulare (HD), 346, 363, 502, 511, 539, 541, 562, 565
 - general aspects, 59, 346, 363, 436, 504
 - intercalatum (HI), 346, 511, 539, 541, 562, 565
 - motor, *see* Wulst, motor
 - nucleus interstitialis hyperpallii apicalis (interstitial part of hyperpallium apicale) (IHA), 346, 510–511, 540–541, 562
 - somatosensory, *see* Wulst, somatosensory
 - visual, *see* Wulst, visual
- Hyperpolarization, 24–25
- Hyperstriatum, *see* Hyperpallium *and* Wulst.
- accessorium, *see* Hyperpallium, apicale (HA)
 - dorsale, *see* Hyperpallium, densocellulare (HD)
 - intercalatus superior (HIS), *see* Hyperpallium, intercalatum (HI)
 - nucleus intercalatus hyperstriatum accessorium, *see* Hyperpallium, nucleus interstitialis hyperpallii apicalis (IHA)
 - ventrale, *see* Mesopallium.
 - caudal medial, *see* Mesopallium, caudomediale (CMM)
 - dorsoventrale, *see* Mesopallium, dorsale (MD)
 - intermediate medial, *see* Mesopallium, intermediomediale (IMM)
 - oval nucleus of, *see* Mesopallium, nucleus ovalis of (MO)
 - ventroventrale, *see* Mesopallium, ventrale (MV)
- Hypocretin, *see* Orexin
- Hypomere, 52, 159, 161, 164
- Hypophyseal portal system, 447
- Hypophysis (Pituitary), 66, 292, 352, 424–425, 446, 448, 451, 453, 457
- Hypothalamus:
- of amniotes, 455–460
 - of anamniotes, 451–456
 - connections (of mammals), 457–460
 - dorsal region (of fishes), 451–452, 454–456
 - general aspects, 65–67, 180, 211, 234, 268–269, 292–294, 296–298, 343, 349–352, 355, 359, 367, 369, 375–378, 421, 424, 430, 433, 435–438, 445–460, 474, 487–488, 507, 511, 552–553, 600–601, 603–605, 611–613, 616, 622, 626, 629, 641, 645, 647, 649, 651, 653
 - inferior lobe, of:
 - cartilaginous fishes, 291, 296–297, 451, 453, 655
 - ray-finned fishes:
 - general aspects, 193–194, 276, 280, 291–293, 296, 298, 380–381, 383, 392, 395, 397–398, 407–412, 453–455, 611, 655
 - nucleus centralis, 453–455
 - nucleus diffusus, 298, 453–455
 - mammillary body (of amniotes), 430, 435, 454–455, 457, 459–561, 622–623, 625–626, 629
 - medial basal, 448
 - nucleus:
 - anterior:
 - of mammals, 455, 457, 461
 - tuberis (of ray-finned fishes), 452
 - arcuate (of mammals), 448, 457, 461
 - dorsolateralis (of reptiles), 458
 - dorsomedial (of mammals), 456–457, 461
 - lateralis:
 - of birds, 459
 - of lungfishes, 455
 - of reptiles, 458
 - lateral(is) posterior(is):
 - of birds, 459
 - of reptiles, 604
 - tuberis:
 - of cartilaginous fishes, 451
 - of ray-finned fishes, 452, 455
 - medial (of fishes), 453
 - medialis posterioris (of birds), 459
 - medius (of sharks), 451
 - paraventricular (of mammals), 448, 455, 457, 461
 - perifornical, 448
 - periventricular(is) (of fishes), 451
 - posterior (of mammals), 455, 457, 461
 - suprachiasmatic:
 - of anamniotes: 433, 451–452, 454
 - general aspects, 409
 - of mammals, 450, 455, 457, 461
 - supraoptic:
 - of birds, 459
 - of mammals, 455, 457, 461
 - tuberis (of birds), 459
 - ventralis:
 - of reptiles, 458
 - tuberis (of ray-finned fishes), 452
 - ventromedial (of mammals), 456–457, 461
- preoptic area (including nuclei), *see* Nuclei, preoptic(us) region:
 - dorsal (of anamniotes), 294, 451, 455–456
 - posterior, 448, 457
 - tuberal, 446, 452, 455
 - ventral (of anamniotes), 294, 451, 455–456
- ventricle, 446
- Hypothesis, *see also* Theory.
- ADVR-claustroramygdalar, 119, 512
 - ADVR-lateral neocortex, 119–120, 512
 - displacement, 117
 - dual elaboration (of dorsal thalamus), 120, 419, 656
 - dual expansion (of dorsal pallium), 656
 - equivalent cell, 118–120, 512, 657
 - field homology (of ADVR), 512
 - handshake, 57
 - invasion, 115, 657
 - inversion, 638, 641, 644
- Hypsiprymnus*, 619
- Ichthyomyzon*, 74, 276, 473, 496, 612
- Ichthyosaurs, 102
- Ictalurus*, 197, 397, 500
- Idiodendrites, 22–23
- Iguana*, 33, 329, 331, 351, 388–389, 412, 426–427, 540–541, 562, 579
- Induction, *see* Evolution/ary, mechanisms, induction
- Induseum griseum, 619
- Inferior, term, 666–667
- Infundibulum:
- of *Branchiostoma*, *see* Cell(s), infundibular (of *Branchiostoma*)
 - of vertebrates, 66, 297, 446–448, 595, 649, 653
- Inhibition, recurrent, 143
- Insectivores, *see* Eulipotyphlans
- Insects (including *Drosophila*), 637–645
- Inside-out, in development of cortex, 56, 510, 656, 658
- Insula, *see* Cortex, insular
- Insulin, 25
- Intelligence:
- and brain size, 106–107, 109
 - evolution of, *see* Evolution, of intelligence
 - general aspects, 108–109

- Interneurons, *see* Neurons, interneurons
- Invasion, *see* Evolution/ary, mechanisms, invasion *and* Hypothesis, invasion
- Invertebrate(s):
- central nervous system:
 - development (embryological), *see* Development, of
 - invertebrate central nervous system
 - organization, 639-641
 - phylogeny, 637-639
 - term, 637-638, 658
- Ion channels, 21
- Ipsilateral, term, 666
- Iris, 217, 652
- Isocortex, term, *see also* Neocortex. 58, 353
- Isodendrites, 22-23
- Isthmus, 267-272, 645
- Jacobson's organ, *see* Organ, vomeronasal
- Janc, J. A., 118
- Jarvis, E. D., 70
- Jaws:
- advent of, 100, 655
 - innervation of muscles of, 134, 206, 208-211
- Jelly fishes, *see* Cnidaria
- Jepsen, G., 117
- Jerison, H., 98, 101, 103, 109
- Jiang, S.-Y., 542
- Johnston, J. B., 69-70, 224
- Jones, E. G., 429, 434
- Kaas, J. H., 44, 118, 505
- Kálmán, M., 89
- Kangaroos, 138
- Karten, H. J., 70, 118-121, 332, 511-512, 657
- Katsuyama, Y., 646
- Kelley, D., 575, 582
- Kenigfest, N., 434
- Kidney, 449, 453, 461
- Killackey, H., 118
- Kinesin, 21
- Kinkajou, 560
- Kinocilium, 32
- Knifefishes, 245
- Krubitzer, L., 118
- Kuhlenbeck, H., 69
- Kulke, F., 561
- Lacalli, T. C., 641, 647-650
- Lacerta*, 61
- Lagomorpha/s, 83, 527-528, 531
- Lamellar body, *see* Body, lamellar
- Lamina(e/r):
- of invertebrates, 639
 - of vertebrates:
 - organization, *see also* Cortex, layers *and* Group I, term. 84
 - organization of optic tectum, *see* Tectum, optic, general organization
 - of spinal cord:
 - general aspects, 129, 147-148
 - Lamina I, 148
 - Lamina II, 148
 - Lamina III, 148
 - Lamina IV, 148, 150
 - Lamina V, 150
 - Lamina VI, 150
 - Lamina VII, 150-152
 - Lamina VIII, 148, 151-152
 - Lamina IX, 148, 151
- term, 261
- Lamination, *see also* Cortex, layers; Group I, term; Lamina(e/r), *and* Tectum, optic, general organization. 102, 147-148, 54-57, 510-511
- Lampetra*, 374, 408, 420
- Lampreys, *see also* *Ichthyomyzon*, *Lampetra*, *and* *Petromyzon*. 74-75, 86, 88, 95-96, 131, 139-141, 197, 214-215, 223-225, 268, 270, 275-276, 281, 283, 285, 290, 293, 303-304, 315-317, 334, 352, 374, 391, 407-408, 410, 414, 418, 420, 432, 446, 451, 472-473, 489, 496, 594, 605-606, 612, 629, 646-648, 651-654
- Lancelet, *see* *Branchiostoma*
- Land, transition to, 136-137
- Lange, W., 97-98
- Language, 581, 587, 589
- LANT6, 471-472, 474, 479, 482-484
- Lanuza, E., 120, 604
- Larsell, O., 69
- Larus*, 217
- Larynx, 582-583, 586-589
- Lateral prominence (of amphibian lateral pallium), 603
- Lateral, term, 61, 666-667
- Latimeria*, *see also* *Crossopterygian*. 76, 78-80, 86-88, 169, 185, 195, 257-260, 281, 283, 304, 407, 414, 497, 595, 597, 653
- Latin, roots of anatomical terms, 668-670
- Lavargheta, A., 542
- Law of the unspecialized, 117
- Leaflet, intergeniculate, *see* Nucleus, intergeniculate leaflet
- Learning, *see* Behavior, learning
- Lemniscus:
- lateral, 68, 195, 269, 272, 274, 279, 296, 575-577
 - lateral line, 304
 - medial, 68, 131, 150, 269, 272-273, 279, 295, 548, 550
 - spinal, 269-270, 272-273, 276, 279, 295, 321
 - trigeminal, 550, 553
- Lemnopallium, *see* Pallium, divisions, lemnopallium
- Lemnothalamus, *see* Thalamus, dorsal, divisions, lemnothalamus
- Lemur:
- flying, 96, 528
 - indri, 357-358, 560
- Lens, 217, 652
- Lepidosauria, term, *see* Lizards, Snakes *and* *Sphenodon*
- Lepisosteus*, 64-65, 78, 276, 292, 318
- Lepomis*, 78, 186, 248, 280, 298, 324, 380, 382-383, 397, 477, 498, 500, 599, 615
- Leptin, 448
- Lepus*, 84, 356
- Leu-enkephalin (Leucine-enkephalin), 25, 142
- Lewis, F. P., 618
- Liem, K. E., 166
- Ligament, denticulate, 150
- Limbic system:
- of amphibians, 612-614, 627-628, 630
 - of birds, 348, 617, 626-630
 - of cartilaginous fishes, 612-613, 615, 628-629
 - general aspects, 66, 109, 407, 411-412, 439, 450, 482-483, 588-589, 611-630
 - of hagfishes, 613, 615, 628
 - of lampreys, 612, 628
 - of lungfishes, 612, 614, 628
 - of mammals, 617-623, 629-630
 - of ray-finned fishes, 612-613, 615-617, 628-630

- of reptiles, 617, 623–627, 629–630
- term, 618, 630
- Lips, 587–589
- Lissauer, *see* Zone of Lissauer
- Lissencephalic/y, 66, 356
- Liver, 463
- Lizards, 41, 61, 95–96, 119, 148, 226, 243–244, 301, 303, 327, 329–332, 351, 362, 385–389, 407, 409, 412, 414, 426–427, 434, 436, 438, 456–458, 488, 502, 511, 539–540, 560–562, 564, 576, 580, 601–603, 624–628
- Lloyd Morgan, C., 107–108
- Lloyd Morgan's Canon, 107–108
- IMAN, *see* Nidopallium, nucleus, lateralis magnocellularis nidopallii anterioris (LMAN)
- Lobe(s), *see also* Lobus.
 - antennal (of invertebrates), 639
 - electrosensory lateral line, 195, 197, 213, 245, 257–260
 - facial, 44–45, 192–194, 210–211, 398
 - frontal, 356–357, 429, 502–504, 587
 - glossopharyngeal, 192–193
 - gustatory, *see also* Lobe, facial *and* Lobe, vagal. 244
 - limbic, 551–552, 618
 - occipital, 356–357, 501–504, 531, 535
 - optic (of invertebrates), 639, 645
 - parietal, 356–357, 502–504
 - temporal, 356–357, 502–504, 587, 623
 - vagal, 192–194, 196, 211, 249
- Lobsters, 641
- Lobus:
 - parolfactorius, of birds, *see* Striatum, mediale.
 - ventromedial part of rostral part, *see* Nucleus accumbens, of birds
 - vocal control region of (in parrot), *see* Striatum, mediale, pars magnocellularis
 - subhippocampalis (of lampreys), 410
 - transitorius, 259
- Locomotion, *see also* Behavior, locomotor.
 - rhythmic, *see also* Command generator. 134, 137–139
 - tetrapod, 137–138
- Locus coeruleus, *see* Nucleus, locus coeruleus
- Locy, W. A., 69, 605
- Lohman, K. J., 313
- Longitudinal, term, 666
- Loops:
 - direct:
 - of birds, 485–487, 489
 - of mammals, 480–482, 485, 489
 - indirect:
 - of birds, 485–487, 489
 - of mammals, 480–485, 489
 - trisynaptic, 620, 622, 626, 630
- Lophius*, 127
- Lophotrochozoa, 638–639
- Lugaro, E., 254
- Luksch, H., 542
- Lungfishes, 76, 78–79, 86–88, 131, 275, 277, 281, 283–284, 290, 292–294, 301, 303, 319, 432, 455–456, 474–475, 497, 595, 605, 612, 614, 628, 653–654
- Luteinizing hormone-releasing hormone (LHRH), *see* Hormone, gonadotropin-releasing (GnRH)
- Luys, J. B., 478
- MacLean, P. D., 114, 618, 630, 649
- Macroevolution, term, 6
- Macrosmatic, term, *see* Olfactory, macrosmatic
- Magnetoreception, *see also* Receptors, magnetosensory. 187–188, 313–314, 409
- Magnification factor, 533
- Mallatt, J., 74–75, 647–652
- Mammalia/s, *see also* Marsupials, *and* Monotremes.
 - general listing, 101, 103, 114, 119–121, 131, 135, 185, 188, 190–191, 198, 200, 205, 208, 213–214, 230, 235, 269, 272, 274–276, 281–285, 290, 292–293, 296–297, 299–301, 303, 305–306, 311, 313–314, 325–328, 330, 332–333, 335, 343–344, 350–351, 353, 355–367, 369, 380, 384–388, 391, 393–396, 407–410, 419–420, 424–425, 429–432, 434–439, 446, 448, 450, 471–472, 476–485, 487–489, 495, 501–512, 514–515, 526, 528, 537–538, 553, 561, 576–577, 580–581, 587, 600–601, 603, 605, 617, 619–624, 626–630, 639–642, 650, 655–658
 - synapsid, *see* Synapsid
 - term, 79–84, 86, 88–89
- Mammillary body, *see* Hypothalamus, mammillary body (of amniotes) *and* Nucleus, mammillary body, of teleosts
- Manacus*, 151
- Manger, P. R., 188, 560
- Marsh, laws, 106–107
- Marsh, O. C., 106
- Marsupials, 80, 83, 86, 152, 235, 303, 361, 434, 504–505, 566, 577, 619
- Martínez-de-la-Torre, M., 417
- Martínez-García, F., 120
- Martínez-Marcos, A., 120, 604
- Masterton, R. B., 118
- Massa caudalis, 145
- Mater:
 - dura, 66
 - pia, 66
- Matrisomes (of cats and monkeys), 479
- Matrix:
 - of dorsal striatum (of mammals), 479, 484
 - periventricular, 84
- McCormick, C. A., 118
- Meador, R. G., 69
- Medial, term, 61, 666–667
- Medina, L., 437, 510–511, 565
- Medulla:
 - of invertebrates, 639
 - of vertebrates, *see* Hindbrain
- Mehler, W., 118
- Melatonin, 37, 448, 450, 586
- Membrane:
 - nictitating, 215
 - postsynaptic, 24
 - tympanic, 214
- Memory:
 - episodic (declarative), 107, 506–507, 514, 516
 - general aspects, 405, 450, 623, 629–630, 639
 - long-term, 611, 620
 - short-term, 506, 611, 620
 - spatial, 628
 - working, 105, 506–507, 514–516
- Mendel, G., 3
- Meninges, *see also* Mater. 66
- Menix, *see also* Meninges.
 - primitive, 66
 - secondary, 66
- Mergus*, 217

- Mesencephalon (Midbrain), general aspects, *see also* Isthmus, Tectum, Tegmentum, *and* Torus. 50, 52–53, 64, 104, 164, 267–274, 640–641, 645, 647–649, 651, 653–655
- Mesocorticolimbic system, 300
- Mesoderm:
- general aspects, 49, 51, 158–159, 161–164, 168–169, 643–644, 652
 - lateral plate, *see* Hypomere
 - paraxial, *see* Epimere
 - prechordal, 49, 55, 168, 650, 652
- Mesomere, 52–53, 159, 161
- Mesopallium (M):
- caudomedial (CMM), 346
 - dorsale (MD), 346
 - general aspects, 346, 363, 502, 507, 511–512, 562, 565, 581
 - intermediomedial (IMM), 346
 - nucleus ovalis of (MO) (in parrots), 346, 584–585
 - ventrale (MV), 346
- Mesostriatal system, 300
- Mesotelencephalic (dopamine) system, 300, 623
- Mesotocin, *see* Isotocin
- Mesulam, M.-M., 488
- Metamorphosis, 37
- Metatheria, term, *see also* Marsupials. 80, 83
- Metencephalon, term, 50, 64, 164
- Met-enkephalin (Methionine-enkephalin), 25
- Metzner, W., 213
- Meyer, A. (Adolf), 69
- Meyer, A. (Axel), 82
- Meynert, T., 69
- Mice, *see* Rodents
- Microevolution, term, 6
- Microtubules, 21
- Midbrain, *see* Mesencephalon
- Midbrain locomotor region, 133, 272, 275–276, 284–285, 298
- Midline, term, 666
- Midsagittal, term, 666–667
- Milk production, 447
- Miller, R. N., 69
- Mitochondria, 21, 23
- mMAN, *see* Nucleus medialis magnocellularis nidopallii anterioris
- Mole rats, blind, 313, 578–579
- Moles:
- general listing, 32, 151, 560, 249–250
 - star-nosed, 32, 34, 36, 44–45, 327–328, 555–556
- Mollusca/s:
- bivalves, 639
 - cephalopods, 637, 639, 642, 657–658
 - general aspects, 638–639
- Molnár, Z., 120, 512
- Monkeys:
- general listing, 62, 83, 95, 527–530, 533–535, 557, 559–560, 578
 - macaque (*Macaca*), 505, 619, 621
 - New World, 83, 96, 105, 557
 - Old World, 83, 96–98, 105, 249, 254, 557, 566
 - owl (*Aotus*), 533
 - rhesus, *see* Monkeys, macaque (*Macaca*)
 - squirrel (*Saimiri*), 98, 359
- Monophyletic, term, 3
- Monotremes, *see also* Platypuses *and* Echidnas. 41, 83, 86, 179, 187–188, 245, 303, 357, 361, 380, 395, 434–435, 504–505, 566, 619
- Morgan's Canon, *see* Lloyd Morgan's Canon
- Mormyrids, 76, 78, 102, 213, 277, 305, 397–398, 658
- Mosasaurs, 102
- Mouse, *see* Rodents
- Mouth, 51, 638, 644
- Movement, voluntary, *see also* Locomotion.
- general aspects, 566
 - grasping, 561, 566
 - rhythmic, 133, 150
- Mpodozis, J., 542
- Mugnaini, E., 258
- Müller, G. B., 12
- Mus*, *see also* Rodents. 355, 477
- Muscle(s):
- branchiomic (branchial), 159, 161–162, 165–166, 168–169, 175, 180, 189, 205–208, 211, 649
 - extensor, 131, 149
 - extraocular, 131, 134, 161–162, 165, 168–169, 175, 179, 185, 205–207, 210, 214–215, 386, 652
 - of the face, 169, 180, 207–210
 - fiber, 141
 - fin, 139
 - flexor, 131, 149
 - hypobranchial, 170
 - intraocular, 215, 463
 - of the jaw, 169, 180, 206, 208–210, 525, 582, 587–589
 - and locomotion, 139
 - pyramidalis, 215
 - quadratus, 215
 - respiratory, 582, 588–589
 - retractor bulbi, 215
 - of the shoulder and neck, 180, 208, 210
 - sonic, 211
 - spindle, 31
 - stapedius, 206, 214
 - tail, 146
 - temporal, 524–525
 - tensor tympani, 206, 214
 - tone, 221, 233
 - tongue, 161–162, 166, 170, 175, 205–210, 321, 604
 - trunk, 146, 149
 - of visceral arches, 165
- Myelencephalon, term, 50, 64, 164
- Myomere, 139
- Myxiniiformes, term, *see also* Hagfishes. 74
- NADPH-diaphorase, 471
- Nares, 40–41, 46
- Natural selection, 3–8, 100
- Nauta, W. J. H., 116, 118, 223
- Navigational strategy:
- allocentric, 616
 - egocentric, 616
- Navodon*, 281, 380
- Neary, T. J., 118, 120, 512
- Necturus*, 78–79, 312
- Němac, P., 313
- Nematoda/es, 638–639
- Neocerebellum, *see* Cerebellum, neocerebellum
- Neocortex, *see also* Cortex *and* Isocortex.
- general aspects, 60, 119, 300, 351, 353–358, 361–365, 432, 478–483, 501–513, 589, 605, 611
 - term, 58, 109, 256
 - size, 104
- Neopterygii, term, 76, 86
- Neostriatum, of:
- birds, *see* Nidopallium (N).
 - caudale, *see* Nidopallium caudale (NC)

- caudolaterale, *see* Nidopallium caudolaterale (NCL)
caudomediale, *see* Nidopallium caudomediale (NCM)
ectostriatum, *see* Entopallium *and* Perientopallium
Field L, *see* Nidopallium, area L pallii
frontale, *see* Nidopallium frontale (NF)
intermedium, *see* Nidopallium intermedium (NI)
magnocellular nucleus of anterior:
 lateral, *see* Nidopallium, nucleus, lateralis
 magnocellularis nidopallii anterioris (LMAN)
 medial, *see* Nidopallium, nucleus, medialis
 magnocellularis nidopallii anterioris (MMAN)
nucleus:
 basalis, *see* Nidopallium, nucleus, basorostralis pallii (Bas)
 caudal, of hyperstriatum ventrale (former incorrect designation), *see* HVC
 central, of the lateral part, *see* Nidopallium, nucleus, centralis nidopallii lateralis (NLC) (in parrots)
 interface, *see* Nidopallium, nucleus, interfascialis nidopallii (Nif)
 oval, of anterior, *see* Nidopallium, nucleus, ovalis nidopallii anterioris (NAO) (in parrots)
mammals, *see* Striatum, dorsal
Nerve(s):
 cord:
 dorsal, *see* Cord, nerve, dorsal
 ventral, *see* Cord, nerve, ventral
 cranial:
 abducens, 168–169, 173–175, 179–180, 206–207, 210, 214–215, 268
 accessory, 170, 174–175, 177, 180, 191, 206, 208, 210–211, 559
 classification of, 157–159, 161–170, 173–175, 177–178, 205–207
 cochlear, *see* Nerve, cranial, octaval
 dorsal:
 facial, 166–169, 174–180, 184, 205–210, 214, 462, 559, 587
 general aspects, 165–166, 173–180, 183–189, 205–209
 glossopharyngeal, 136, 167–169, 174–180, 184, 191, 206, 208–211, 462–463, 583
 of head segment, 166–170
 vagus, 134, 136, 167–168, 170, 173–180, 184, 191, 206, 208–211, 462, 587
 dorsolateral:
 general aspects, 165–166, 168, 178, 183–184, 191, 194–200
 of head segment, 167–170
 embryological origin, 162–164, 174–175
 epiphyseal, 136, 166, 168, 174–175, 180, 407, 409
 facial, *see* Nerve, cranial, dorsal, facial *and* Nerve, cranial, ventrolateral, facial
 ganglia of, *see individual listings under* Ganglia/on
 general aspects, 64, 157–170, 173–181
 glossopharyngeal, *see* Nerve, cranial, dorsal, glossopharyngeal *and* Nerve, cranial, ventrolateral, glossopharyngeal
 hypoglossal, 170, 174–175, 177, 179–180, 205–207, 209–210, 587
 lateral line:
 anterodorsal, 168–169, 179, 185–186, 195–196
 anteroventral, 168–169, 179, 195–196
 general aspects, 168–169, 174, 177–179, 184, 194–196, 242–244
 middle, 168–169, 179, 195–196
 otic, 168–169, 179, 195
 posterior, 168–169, 179, 195–196
 supratemporal, 168–169, 179, 195–196
 motor, 205–218
 octaval, 68, 168–169, 173–175, 178, 184, 194, 196, 211, 216, 247, 249, 254–255, 258, 261
 oculomotor, *see also* Complex, oculomotor *and* Neurons, oculomotor. 168, 173–175, 177, 179–180, 205–207, 209–210, 214–216, 269, 273, 279, 292–293, 296, 649
 olfactory, 64, 66, 168, 174–175, 180–181, 593–596, 606, 649, 652, 655
 optic, 64, 68, 136, 166, 168, 173–175, 180, 268–269, 344, 362, 452, 457, 523–524, 527
 parasympathetic, *see* Autonomic nervous system, parasympathetic division
 parietal, *see* Nerve, epiphyseal
 praepreticus, 605
 profundus, 168, 174–175, 177–178, 180, 185
 segmental organization of, 166–170
 sensory, 32, 183–200
 somatic afferent, general aspects, 129, 175, 178, 183–200
 somatic efferent, general aspects, 129, 175, 206–208, 210
 spinal, 132
 spinal accessory, *see* Nerve, cranial, accessory
 terminal, 41, 163, 168, 174–175, 180–181, 593, 605, 649, 652, 655
 trigeminal, 33, 38, 168–169, 173–180, 183–190, 205–210, 214–215, 245, 247, 276, 279, 281, 295, 548, 559, 566, 587
 trochlear, 168–169, 174–175, 177, 179–180, 206–207, 210, 214–215
 vagus, *see* Nerve, cranial, dorsal, vagus *and* Nerve, cranial, ventrolateral, vagus
 ventral, of head segment, 165–166, 168–169, 173, 205–207, 210
 ventrolateral:
 facial, 166–169, 174–175, 178–179, 181, 184, 190–193
 general aspects, 165–166, 168–170, 174–176, 178–179, 181, 183–184, 189–194
 glossopharyngeal, 167–168, 170, 174–175, 178–179, 181, 184, 190–193
 of head segment, 166–170
 vagus, 167–168, 170, 174–175, 178–179, 181, 184, 190–193
 vestibular, *see* Nerve, cranial, octaval
 vestibulocochlear, *see* Nerve, cranial, octaval
 visceral afferent, general aspects, 132, 175, 178, 184
 visceral efferent, general aspects, 132, 175, 206, 209–210
 vomeronasal, 168, 174–175, 180–181, 595, 597, 601, 606
 endings, free, 31–32, 42
 net (of hemichordates), 645
 rostral (of *Branchiostoma*), 647–649
 spinal, general aspects, 63–64, 157
Neural:
 crest, 54–55, 61, 135, 158, 161–164, 167–168, 174–175, 181, 185, 605, 644, 649, 651–653, 657–658
 fold, 50–52, 161
 plate, 50–51
 surface, *see* Surface, neural
 tube, 50–52, 55, 135–136, 161–162, 168, 174–175, 643, 649
Neuroactive substances, *see also* Neuropeptides. 24–26, 134
Neuroblasts, *see* Cell(s), neuroblasts
Neurocord, 645
Neurogenesis, 54

- Neurohypophysis:
 general aspects, 145, 446–448, 453, 457
 hormones, *see* Oxytocin *and* Vasopressin
- Neurokinin, 552
- Neuromast, *see* Receptors, neuromast
- Neuromere/ic, 53, 164–166, 657
- Neuromodulator(s), 21, 24–25
- Neuronal nitric oxide synthase (nNOS), 471–472
- Neuronal tracing techniques, *see also* Stains.
 anterograde degeneration, 28–29
 autoradiography, 28–29
 axonal transport, 28–29
 cholera toxin, 29
 double-labeling, 28
 fluorescent dyes:
 Di-I and Di-O, 29
 Evans blue, 29
 fast blue, 29
 fluorogold, 29
 gene expression, 28
 general aspects, 27–28
 horseradish peroxidase (HRP), 28–29
 immunohistochemistry, 28–29
 Phaseolus vulgaris leucoagglutinin (PHA-L), 28–29
 retrograde degeneration, 28
 rhodamine beads, 29
 toxins, 29
 wheat germ agglutinin, 28–29
- Neuronal transport:
 anterograde:
 fast, 21
 slow, 21
 general aspects, 21, 28
 retrograde, fast, 21
- Neuron(s), *see also* Cell(s).
 afferent, 62–63
 allodendritic, 22
 bipolar, sensory, 162
 cholinergic, *see* Acetylcholine/cholinergic *and/or*
 Acetylcholinesterase (AChE) *and* Choline
 acetyltransferase (CHAT)
 classification, 21–23, 62–63
 effector, *see* Neurons, motor
 efferent, 62–63
 electromotor, 144, 212
 first-order multipolar (FOMs), 68, 134
 general aspects, 19–20, 62–63
 giant reticulospinal, 223–224
 Golgi:
 Type I, 26–27, 62–63, 102, 223
 Type II, 27, 62–63
 identifiable, 95
 idiiodendritic, 22
 interneurons, 27, 62, 140, 143, 645
 isodendritic, 22, 116
 juxtalemniscal, 213
 local circuit, 27, 62
 motor:
 general aspects, 141, 149
 primary, 141, 143
 secondary, 141
 ventrolateral column of, *see* Column, ventrolateral
 ventromedial column of, *see* Column, ventromedial
 multipolar, 22
 paraventricular, of octaval column, 212
 projection, 62
 reticular formation, 223
 somatosensory, 46
- Neuropeptides, 448
- Neuropeptide Y, 25, 142, 448, 471–472, 476
- Neuropil:
 of Bellonci, 350, 433–434
 dorsomedial (of lampreys), 408, 496, 594, 612
- Neuropore, 648
- Neurotaxonomy, 104
- Neurotensin, 25
- Neurotransmitter(s):
 cholinergic, 25
 general aspects, 21, 24–25
 reuptake, 24
- Newts, *see* Urodela/es
- Nguyen, A., 542
- Nicholson, C., 118, 224
- Nidopallium (N), *see also* Entopallium *and* Perientopallium.
 area L pallii (L), 347, 363, 426, 576, 580–581, 584–585, 587
 caudale (NC), 347, 561
 caudolaterale (NCL), 347, 513–516
 caudomediale (NCM), 347
 frontale (NF), 347, 561, 584–585
 general aspects, 347, 363, 502, 507, 511–512, 514, 540,
 561–562, 565–566, 580
 HVC, *see* HVC
 intermedium (NI), 347, 563–565
 nucleus:
 basorostralis pallii (basorostral pallial) (Bas), 187, 347, 363,
 488, 561–563, 565, 584–585
 centralis nidopallii lateralis (central nucleus of the lateral)
 (NLC) (in parrots), 347, 584–585
 entopallialis, *see* Entopallium
 interfacialis nidopallii (interface nucleus) (Nif), 347,
 584–585
 lateralis magnocellularis nidopallii anterioris (lateral
 magnocellular of anterior nidopallium) (LMAN),
 347, 584–586
 medialis magnocellularis nidopallii anterioris (medial
 magnocellular of anterior nidopallium) (MMAN),
 347
 ovalis nidopallii anterioris (oval nucleus of anterior
 nidopallium) (NAO) (in parrots), 347, 584–585
- Nielsen, C., 644
- Nieuwenhuys, R., 26, 118, 224, 260
- Nigrostriatal dopamine system, 300
- Nitric oxide, 142, 462, 586
- Nociception, *see* Receptor, pain *and* Receptor, general chemical
- Noden, D. M., 158, 166
- Nomenclature:
 derivation, 668–670
 descriptive, 70, 364
 directional terms, 665–667
 general aspects, 69–70, 344, 364, 378–379, 396, 397
 glossary of terms, 671–677
 of hippocampal formation, *see* Hippocampus, nomenclature
 revised avian, *see also* Avian Brain Nomenclature Forum. 70,
 268, 344–348, 363, 368
- Nontetrapods, *see also* Actinopterygians, Chondrichthyans,
 Crossopterygian, Hagfishes, Lampreys, *and*
 Lungfishes. 139
- Noradrenaline, *see* Norepinephrine
- Norepinephrine (Noradrenaline), 25, 142, 230–231, 232, 235,
 255, 272, 278, 462–463, 552, 586
- Northcutt, R. G., 10–11, 118, 121, 164, 166, 649, 652, 657
- Nostrils, *see* Nares

- Notochord, 49, 51–52, 55, 161, 644–645, 647, 651–652
 Notopterid, 76, 78, 305, 397
Notorynchus, 77
 Nübler-Jung, K., 641
 Nuclear group (of dorsal thalamus of mammals):
 anterior, *see also* Nucleus, anterior, of monotremes, 419, 430–431, 434–435, 438, 510, 622–623
 intralaminar:
 caudal (collothalamic), 419, 430–432, 437–438
 general aspects, 424–425, 435–437, 479–485, 487, 489, 510
 rostral (lemnthalamic), 419, 430–431, 434, 438–439
 lateral, 429–430
 medial, 419, 430, 434–435, 438–439, 510, 622
 midline, 430, 434, 437
 posterior, 326, 333, 335, 419–420, 425, 429–430, 437–438, 508–509, 537–538, 543, 548, 551–552
 ventral (ventrobasal/ventrolateral complex), 419, 429, 431, 434–435, 438–439, 479, 548, 551–553
 Nucleus of cell, 20
 Nucleus/ei of central nervous system
 abducens, 206–207, 210, 216, 234, 236, 375, 391, 463
 accessory:
 basal, of amygdala, *see* Amygdala, accessory basal nucleus
 olfactory tract, of, 456
 spinal, 206, 208, 210
 accumbens, *see also* Striatum, ventral.
 of anamniotes, 364, 474–475, 603, 612
 of birds, *see also* Nucleus striae terminalis lateralis, 345, 487
 core and/or shell organization, 479, 483
 general aspects, 477
 of mammals, 233, 297, 300–301, 365–367, 471, 476, 478–479, 483, 511, 600, 620, 629
 of reptiles, 368–369, 484, 604, 626
 A cell groups of Dahlström and Fuxe, *see* Cell groups, A
 ambiguus, 191, 206, 208, 210–211, 559, 587–588
 amygdalar, *see* Amygdala
 angularis (cochlear recipient), 198, 573–574, 576
 anterior:
 of ansa lenticularis (of birds), *see* Nucleus, subthalamic, of birds
 cortical, of amygdala, *see* Amygdala, anterior cortical nucleus
 of dorsal thalamus (of jawed fishes and amphibians), 318–320, 322, 325, 335, 350, 375, 410, 418, 420–423, 432–434, 437–438, 455, 498–499, 575, 583, 613, 653, 658
 entopeduncular:
 of amphibians, 474–475
 of reptiles, *see* Nucleus, subthalamic, of reptiles
 of hagfishes, 422, 434
 of hypothalamus, *see* Hypothalamus, anterior nucleus
 lateral (of amphibians), 320, 422, 427, 430, 437
 of monotremes, 435, 438
 of octaval column, 197–198, 276
 olfactory (of mammals), 366
 paraventricular, of habenula, *see* Habenula, of mammals, anterior paraventricular nucleus
 tuberis, 212
 anterodorsal:
 of mammals, 424, 430, 435
 tegmental (of amphibians), 321
 anteromedial (of mammals), 424, 430, 435
 anteroventral (of mammals), 424, 430, 435
 anteroventral cochlear (of mammals), 198
 a (of skates), 598
 A (of sharks), 594–595, 612
 B, 227
 basal(is):
 of amygdala, *see* Amygdala, frontotemporal division of anamniotes (cholinergic cell group), 489
 of birds (trigeminal target), *see* Nidopallium, nucleus, basorostralis pallii
 general aspects, 489
 magnocellularis (of birds, cholinergic cell group), 345, 369, 488
 of mammals (of Meynert, cholinergic cell group, magnocellular corticopetal cell complex), 364–367, 474, 477, 488–489
 of reptiles (cholinergic cell group), 488
 basal optic nucleus, of:
 nonteleost ray-finned fishes, 391
 sharks, 391–392
 of the basal optic root, of:
 amphibians, 377, 391, 396
 birds, 302, 313, 390–391, 394–395
 reptiles, 394–395
 basolateral, of amygdala, *see* Amygdala, basolateral division
 basorostralis pallii, *see* Nidopallium, nucleus, basorostralis pallii
 B cell groups of Dahlström and Fuxe, *see* Cell groups, B
 of Bechterew, 385–386, 393–394
 bed, of:
 hippocampal commissure (of amphibians), 410
 pallial commissure (of amphibians), 612–613
 stria terminalis:
 of anamniotes, 354, 475, 488, 603
 of birds, 369, 487, 489
 of mammals, 345, 359, 365, 367, 487–489
 of reptiles, 361, 368–369, 484, 488–489
 of Bellonci (of amphibians), 350, 433
 bulbar command associated, 213
 of Cajal, 217–218
 caudal(is):
 of hyperstriatum ventrale, *see* HVC
 of lateralis column, 195
 neurosecretory, 145
 of turtles, *see* Nucleus, medial(is) posterior, of lizards
 of ventral octaval column, 198
 caudate, *see* Nucleus, caudate-putamen
 caudate-putamen, 297, 300, 355, 358–360, 364–367, 424, 471, 476–484, 543, 619, 621
 central(is):
 of amphibians, 422, 427
 of amygdala, *see* Amygdala, nucleus, central
 arcopallii anterioris (AAC), *see* Arcopallium, nucleus, centralis arcopallii anterioris (AAC) (in parrots)
 of cartilaginous fishes, *see* Pallium, central nucleus (of sharks)
 of dorsal thalamus (of amphibians), 455
 of inferior lobe, *see* Hypothalamus, inferior lobe, nucleus centralis
 lateral(is), 430–431, 436, 438, 479, 551–552
 median, 430, 436, 487
 nidopallii lateralis (NLC), *see* Nidopallium, nucleus, centralis nidopallii lateralis (NLC) (in parrots)
 posterior:
 lateral (of amphibians), 476
 of teleosts, 211–212, 292, 305, 418, 420–421, 423, 437
 thalamic, of amphibians, 294, 422, 476, 575

- zone, of dorsal telencephalic area (of ray-finned fishes),
see Area, dorsal telencephalic (D), central zone
of (Dc)
- centre médian (centromedian), 430, 436, 551
- cerebellar (of gars), 276
- circularis, 388–389
- cochlear, 44, 179, 184, 258, 305, 573, 577, 581, 587
- command, 213
- commissural, of ventral telencephalic area (of ray-finned fishes), see Area, ventral(is), telencephalic, nuclei of, commissural (Vc)
- corpus geniculatum thalamicum (of frogs), 433–434
- corticalis, of:
gars and bowfin, 375–376
teleosts, 379–383, 393, 453
- corticomedial, see Amygdala, corticomedial division
- cuneatus, 131, 135, 150, 258, 548
- cuneiform(is):
of cartilaginous fishes, 279, 284, 296
general aspects, 224, 228–230, 269, 272
of mammals, 272, 299, 352, 435
- of Darkschewitsch, 217–218, 384–386, 394
- deep, of cerebellum, see Cerebellum, deep nuclei
- dentate, 261
- descending:
of octaval column, 197, 212
of trigeminal, see Nucleus, trigeminal, descending
vestibular (of nonmammalian amniotes), 198, 200
- of the diagonal band of Broca (diagonalis Brocae), see Septum, nucleus, of the diagonal band of Broca
- diffusus, of inferior lobe, see Hypothalamus, inferior lobe, nucleus diffusus
- dorsal(is):
accessory optic, of:
bowfin, 376
teleosts, 379, 392–393
- cap of Kooy, 393
- cochlear (of mammals), 198
- column, see also Nucleus, gracilis and Nucleus, cuneatus.
68, 135, 150, 321, 385, 429–430, 433, 435–436,
438, 507–508, 548, 550–551, 553, 560, 562–563
- electroreceptive, 195
- intermedius ventralis anterior (DIVA) (of birds), 428, 431,
436, 438, 507–508, 560, 563
- lateral geniculate:
of birds, 330, 335, 428, 431, 436, 438, 507–508,
538–539, 543
evolution of, 527–529
lamination of, 526–529
of mammals, 282, 299, 326, 335, 351, 384–385,
393–395, 419, 424–425, 429, 431, 434, 436,
439, 507–509, 524–525, 527–528, 533, 537,
577–578, 621
of reptiles, 329, 335, 426, 436, 438, 507–508, 538–539,
543, 623
- lateral optic, 436
- medullary (of frogs), 575
- motor, of vagus, 191, 206, 209–210, 233, 457, 463, 487
- octavolateralis (electrosensory), 195, 317
- of posterior commissure (of reptiles), 328–329, 334,
386–388, 484–485
- posterior, of teleosts, 318–319, 322, 325, 335, 418,
420–421, 423, 427, 430, 437
- pretectal (of reptiles), see Nucleus, lentiformis, thalami (of reptiles), dorsal pretectal nucleus
- tegmental, of hagfishes, 279, 294–295
- terminal (of mammals), 384, 393–396
- of ventral telencephalic area (of ray-finned fishes), see Area, ventral(is), telencephalic (V), nuclei of, dorsal (Vd)
- zone, of dorsal telencephalic area (of ray-finned fishes), see Area, dorsal telencephalic (D), dorsal zone of (Dd)
- dorsointermedius posterior (of birds), 428, 431, 437–438,
485, 566
- dorsolateral(is):
anterior:
general aspects, 560–561, 563
pars magnocellularis, of OPT complex (of birds), see Nucleus, dorsal(is), lateral geniculate, of birds
of reptiles, 419, 426–427, 431, 436–438, 484, 510,
625–626, 629
thalami (of birds), 428, 431, 436–438, 485, 510, 566
thalami pars medialis (of birds), 428, 431, 436–438
- of dorsal octaval column, 198
- of OPT complex (of birds), see Nucleus, dorsal(is), lateral geniculate, of birds
- pontine (of mammals), 385–386
- posterior:
of birds, 431, 437–438, 514
caudal part (cDLP) (of birds), 428, 431–432, 508–509,
562, 564, 585
- tegmentum, 323
- vestibular (of nonmammalian amniotes), 198, 200
- dorsomedial(is):
anterior (of birds), 428, 431, 436–438, 485, 510, 514, 566,
601
of midbrain, 584, 588–589
posterior (of birds), 428, 431, 437
of reptiles, 419, 426–427, 431, 436–438, 484, 510
- ectomamillaris (of birds), see Nucleus, of the basal optic root, of birds
- Edinger-Westphal, 206, 209–210, 215, 217, 284, 375,
384–385, 387, 395–396
- electrosensorius (of teleosts), 212, 298, 305, 397–398, 501
- emboliformis, 261
- endopiriform, 358–360
- entopallialis, see Entopallium
- entopeduncular:
of amphibians, 364, 595
of mammals, 365, 411
of ray-finned fishes (including rostral, Er, and caudal, Ec),
410, 500
- external (of hagfishes):
of preoptic area, see Nucleus, preoptic(us), external (of hagfishes)
of dorsal thalamus, 418, 422
- externus (of birds), 352
- F, 227
- facial, see Nucleus, motor, of dorsal facial nerve
- fastigial, 261, 386
- of field H of Forel, see Nucleus, reticular(is), subthalamic
- funicular, 256
- geniculate, dorsal lateral, see Nucleus, dorsal(is), lateral geniculate
- geniculate, medial, see Nucleus, medial(is), geniculate
- geniculatus pretectalis, see Nucleus, pretectal(is), geniculatus
- globosus, 261
- globus pallidus, see Pallidum, dorsal (globus pallidus)
- glomerulosus, 298, 380–381, 383, 392, 453, 605, 658
- gracilis, 131, 135, 150, 548

- griseus tectalis, *see* Nucleus, tectal gray
- gustatory:
- general aspects, 179, 184, 190, 429, 454
 - secondary, 276, 278, 398–399
 - superior secondary, 193–194
 - tertiary, 193–194, 398, 454
- habenular, *see* Habenula
- H (of cartilaginous fishes), 279, 290–291, 296
- HVC, *see* HVC
- hypoglossal:
- general aspects, 206–207, 209–210, 321, 582–583, 587–589, 604
 - tracheosyringeal division of, 582, 585–586, 589
- inferior:
- olivary/olive:
 - principal division, 242, 256, 259, 261, 385–386, 393–394, 564, 566
 - accessory, 256 - salivatory, *see* Nucleus, salivatory, inferior
 - vestibular (of mammals), 200
- infundibular, 451–452, 583
- intercalatus:
- hyperstriatum accessorium, *see* Hyperpallium, nucleus
 - interstitialis hyperpallii apicalis (IHA)
 - superior, of hyperstriatum (HIS), *see* Hyperpallium, intercalatum (HI)
 - thalami, term, 436
- intercollicular, of:
- cartilaginous fishes, 284
 - reptiles, 301
- interface, of the neostriatum, *see* Nidopallium, nucleus
- interfacialis nidopallii (Nif)
- interfacialis nidopallii, *see* Nidopallium, nucleus, interfacialis nidopallii (Nif)
- intergeniculate leaflet, 350–351, 394
- intermediate, of ventral telencephalic area (of ray-finned fishes), *see* Area, ventral(is), telencephalic, nuclei of, intermediate (Vi)
- intermedius, of:
- birds, 209
 - lateralis column, 195
 - ventral thalamus of fishes, 350
- internal (of hagfishes), 418, 422
- interpeduncular, 227, 269–272, 275–276, 278–280, 282, 285, 290, 296–297, 299–302, 346, 384, 392, 407, 409–413, 629
- interpositus, 260
- interstitial, of:
- basal forebrain bundle (of cartilaginous fishes), 473
 - Cajal, 384–386, 394
 - medial longitudinal fasciculus, 269, 279, 293–294, 296, 321, 392–393
 - posterior commissure (of turtles), 387
- interstitio-pretectalis-subpretectalis (of birds), 387, 390–391, 395
- intracollicularis, 391
- intrapeduncularis (of birds), 345, 363, 485, 487
- isthmi:
- of birds, 271, 282–283, 302, 456
 - of cartilaginous fishes, 322
 - general aspects, 269–272, 275–276, 280–283, 312, 317–318, 320–321, 323, 325–326, 328, 330, 334, 379–381, 392–393
 - pars magnocellularis, 271, 282–283, 302
 - pars parvocellularis, 271, 282–283, 302
 - pars semilunaris, 283
- isthmo-optic, 271–272, 275, 283–284, 330
- K (of cartilaginous fishes), 290, 297
- laminaris, 198–199, 573–574, 576
- laminaris precommissuralis (of birds), 390–391
- laminar, of torus semicircularis (of amphibians), 575
- lateral(is):
- of amygdala, *see* Amygdala, nucleus, lateral
 - anterior (of birds), 352
 - dorsal:
 - of *Bombina* (a frog), 433
 - of mammals, 424–425, 430, 435 - of frogs, 575
 - geniculate:
 - pars dorsalis, *see* Nucleus, dorsal, lateral geniculate
 - pars ventralis, *see* Nucleus, ventral, lateral geniculate - of habenula, *see* Habenula, of mammals, lateral nucleus
 - mesencephalic:
 - of birds, *see* Nucleus, mesencephalic(us), lateralis, pars dorsalis
 - of Group I cartilaginous fishes, 195, 304, 317
 - nuclear complex (of Group II cartilaginous fishes):
 - anterior nucleus, 296–297, 305
 - dorsomedial nucleus, 279, 296, 305
 - general aspects, 195, 279, 296, 305
 - lateral nucleus, 279, 296, 305
 - ventromedial nucleus, 279, 296, 305 - magnocellularis of the anterior neostriatum (IMAN), *see* Nidopallium, nucleus, lateralis magnocellularis
 - nidopallii anterioris (LMAN)
- octaval, 198
- ovalis mesopallii, *see* Mesopallium, nucleus, ovalis
- ovalis nidopallii anterioris, *see* Nidopallium, nucleus, ovalis nidopallii anterioris
- posterior (electrosensory, of skates), 499
- posterior/pulvinar complex (of mammals), 282, 326, 333, 335, 384–385, 393, 395, 419, 424–425, 429–432, 437, 439, 508–509, 536–538, 543
- posterior thalamic:
- of frogs, 294
 - of skates, 613
- septal, *see* Septum, lateral nuclei
- spiriform (of birds), 282, 284–285, 302, 329, 335, 386–387, 390–391, 395–396, 485
- superior olive, 198
- tegmental, 292, 322
- terminal (of mammals), 384, 393–396
- thalamic:
- of amphibians (including posterodorsal division), 375, 377
 - of teleosts, 381, 399
- trigeminal, of:
- bats, *see* Nucleus, trigeminal, lateral, of bats
 - snakes, *see* Nucleus, trigeminal, lateral, of snakes
- valvulae, 242, 256, 318, 380–381, 392–393, 454
- of ventral octaval column, 198
- of ventral telencephalic area (of ray-finned fishes), *see* Area, ventral(is), telencephalic (V), nuclei of, lateral (VI)
- vestibular, 198, 200
- zone, of dorsal telencephalic area (of ray-finned fishes), *see* Area, dorsal telencephalic (D), lateral zone of (DI)
- of lateral lemniscus, 198, 305, 575–577
- laterodorsal tegmental, 284, 456
- lentiform, *see also* Globus pallidus and Nucleus, caudate-putamen. 365, 367, 369
- lentiformis:
- mesencephali, of:

- anurans, 375, 377, 391
- birds, 387, 390–391, 395–396
- reptiles, 385–388, 391, 394–396
- thalami (of reptiles):
 - dorsal pretectal nucleus, 385, 389
 - medial pretectal nucleus, 385, 389
 - pars extensa, 385, 388–389
 - pars plicata, 385, 388–389
- limitans/suprageniculate (of mammals), 333, 384, 429–431, 509, 537, 548–550
- lobi lateralis, 451
- lobobulbaris, 398
- locus coeruleus, 226–230, 232–233, 236, 255–256, 268–269, 271–272, 275–278, 280–281, 317, 323, 454, 550, 622, 626, 629
- magnocellular(is):
 - of anterior neostriatum, *see* Nidopallium, nucleus, lateralis magnocellularis nidopallii anterioris (LMAN) *and* Nidopallium, nucleus, medialis magnocellularis nidopallii anterioris (MMAN)
 - cochlear-recipient, of brainstem, 198–199, 249, 573–574, 576
 - corticopetal cell complex, *see* Nucleus, basalis, of mammals
 - of dorsomedial thalamus (of birds), 584–585
 - of octaval column, 197
- mammillary body:
 - of amniotes, *see* Hypothalamus, mammillary body (of amniotes)
 - of teleosts (goldfish), 380–381, 399
- of marginal optic tract (of birds), 352
- medial(is):
 - of amygdala, *see* Amygdala, medial nucleus
 - of cerebellum (of birds), 260–261
 - complex (of crocodiles), *see* Nucleus, medial(is), posterior, of lizards
 - geniculate (of mammals):
 - general aspects, 299, 305, 384, 419–420, 424–425, 429, 431, 437, 509–510, 576–577, 579–581, 621
 - pars dorsalis, 420, 429
 - pars magnocellularis (medialis), 420, 429, 431
 - pars ventralis, 305, 420, 429
 - of habenula, *see* Habenula, of mammals, medial nucleus
 - of lateralis column, 195
 - of lizards (nucleus reuniens, pars compacta), 419–420, 427, 431, 437, 509–510, 562, 576, 580–581
 - magnocellularis of the anterior neostriatum (mMAN), *see* Nidopallium, nucleus, medialis magnocellularis nidopallii anterioris (MMAN)
 - pretectal (of reptiles), *see* Nucleus, lentiformis, thalami (of reptiles), medial pretectal nucleus
 - posterior, of lizards (nucleus medial(is) complex of crocodiles, nucleus caudalis of turtles), 419, 427, 431–432, 437, 508–509
 - septal, *see* Septum, medial nuclei
 - spiriform (of birds), 282, 302, 387–391, 395, 511
 - superior olive (of mammals), 198
 - terminal (of mammals), 384, 391, 393–396
 - vestibular, of:
 - anurans, 198
 - birds, 198, 200
 - mammals, 200
 - zone, of dorsal telencephalic area (of ray-finned fishes), *see* Area, dorsal telencephalic (D), medial zone of (Dm)
- median central, 430
- medianus, of the posterior tuberculum, *see* Tuberculum, posterior, nucleus medianus
- mediodorsal:
 - of monotremes, 435, 438
 - of therian mammals, 300, 424–425, 430–431, 434–435, 437–438, 482, 487–488, 502, 504, 510, 514, 600
- medioventral (reuniens) (of mammals), 424–425, 430, 435, 488, 622
- medullary electromotor relay, 213
- mesencephalic(us):
 - command associated, 213
 - lateralis, pars dorsalis, 271, 274, 302, 306, 510
 - tegmental (of frogs), 294
 - of the trigeminal nerve, *see* Nucleus, trigeminal mesencephalic
- motor, of:
 - dorsal facial nerve, 186, 206, 208, 210, 559, 587–589
 - trigeminal nerve, *see* Nucleus, trigeminal, motor
- 'nother, of ventral telencephalic area (of ray-finned fishes), *see* Area, ventral(is), telencephalic, nuclei of, 'nother (Vn)
- N (of sharks), *see* Nucleus, A
- octaval anterior, 227
- octavolateral, 321–323
- octavomotor (of octavis column), 197
- oculomotor:
 - electromotor division (in stargazer), 217
 - somatic components, 206–207, 210, 216–217, 234, 236, 247, 269–271, 273, 279, 284, 290, 293, 296–299, 301–302, 321, 384–386, 391–395, 407, 463, 558
- olfactoretinalis (of ray-finned fishes), 605
- olivary/olive:
 - inferior, *see* Nucleus, inferior, olivary/olive
 - superior, *see* Nucleus, superior, olivary
- of Onuf, 151
- optic, of posterior commissure, *see* Nucleus, pretectal(is), periventricular, dorsal
- of the optic tract (of mammals), 380, 384, 387, 391, 393–396
- opticus pretectalis ventrolateralis (of turtles), 387
- opticus principalis thalami, *see* Complex, opticus principalis thalami (OPT) *and* Nucleus, dorsal(is), lateral geniculate, of birds
- ovalis:
 - mesopallii, *see* Mesopallium, nucleus ovalis of nidopallii anterioris, *see* Nidopallium, nucleus, ovalis nidopallii anterioris
 - of reptiles, 350
- ovoidalis:
 - of birds, 390–391, 426, 428, 431–432, 437, 509–510, 576, 580–581, 587
 - ventromedial part (of birds), *see* Nucleus, semilunaris parovoidalis
- pacemaker (of teleosts), 211–212, 501
- parabigeminal, 272, 282–283, 299, 326
- parabrachial, 190, 192–193, 234, 236
- paracentral, 430–431, 436, 438
- paracommissuralis (of teleosts), 256, 325, 378, 393
- parafascicular(is), 430–431, 436, 438, 479, 485, 551–552
- paralaminar, of amygdala, *see* Amygdala, paralaminar nucleus
- parataenial (of mammals), 424–425, 430, 435
- paraventricular (of mammals), 424–425, 430, 622
- of paraventricular organ, 454
- pedunculopontine, 224, 226, 228–230, 233–234, 282, 284–285, 297, 300, 302–303, 430
- periglomerular, 454

- peripeduncular, 431
- peritondal (of nonmammalian amniotes), 431, 436
- pontine, 135, 255–256, 261, 281, 299, 388, 478, 551, 559–560, 564, 566
- population, 26
- postcommissural, of ventral telencephalic area (of ray-finned fishes), *see* Area, ventral(is), telencephalic, nuclei of, postcommissural (Vc)
- of the posterior commissure, of:
 - anurans, 375, 377
 - hagfishes, 283, 375, 378
 - mammals, 217, 384, 394
 - reptiles, 385
- posterior(is):
 - amygdalopallii, *see* Amygdala, nucleus, posterioris amygdalopallii
 - of ansa lenticularis (of birds), 387, 390–391
 - cortical, of amygdala, *see* Amygdala, posterior cortical nucleus
 - group, *see* Nuclear group (of dorsal thalamus of mammals), posterior *and* Nucleus, limitans/suprageniculat
 - intralaminar, 420, 429, 431–432
 - lateral part (Pol) (of mammals), 431
 - medial part (Pom) (of mammals), 548–550
 - lateral (of amphibians), 422, 427
 - lateral thalamic (of cartilaginous fishes), 374, 378, 392, 396, 612
 - of octaval column, 197
 - paraventricular, of habenula, *see* Habenula, of mammals, posterior paraventricular nucleus
 - pretectal:
 - of mammals, 326, 335
 - of teleosts, *see* Nucleus, pretectal(is), posterior, of, teleosts
 - thalamic nucleus, of:
 - anurans, 294, 375, 377, 418, 422, 575
 - ray-finned fishes, 193–194, 398–399
 - of turtles, 386–388
 - zone, of dorsal telencephalic area (of ray-finned fishes), *see* Area, dorsal telencephalic (D), posterior zone of (Dp)
- posterodorsalis (of reptiles), 385–386, 388
- posteroventral cochlear (of mammals), 198
- posteroventral (of reptiles), 456
- praetectalis:
 - olivaris (of urodeles), 375
 - profundus (of urodeles), 375
- precommand, 213
- preeminentialis, 259–260
- pregeniculate (of primates), *see also* Nucleus, ventral, lateral geniculate (of amniotes), 350
- preglomerular, *see* Preglomerular nuclear complex
- preoptic(us), *see also* Area, preoptic.
 - dorsal(is) (of hagfishes), 451–452
 - external/us (of hagfishes), 451–452
 - intermediate/us (of hagfishes), 451–452
 - magnocellularis (of ray-finned fishes), 451–452, 454
- medial(is):
 - of birds, 457, 459
 - of mammals, 457
- paraventricularis magnocellularis (of birds), 459
- parvocellularis:
 - anterioris (of ray-finned fishes), 451
 - general area, 212
 - posterioris (of ray-finned fishes), 452, 454
- periventricular(is):
 - of hagfishes, 451–452
 - magnocellularis (of birds), 459
 - of reptiles, 458
- prepacemaker (of teleosts), 212, 305, 501
- pretectal(is), *see also* Area, pretectalis; Nucleus, lentiformis, mesencephali; Nucleus, lentiformis, thalami; *and* Nucleus, praetectalis.
 - anterior (of mammals), 380, 384–387, 394, 396
 - of birds, 302, 387, 390
 - central, of:
 - cartilaginous fishes, 374, 378, 392
 - non-teleost ray-finned fishes, 375–376
 - teleosts, 378–379, 393
 - of crocodiles, 387
 - diffusus (of birds), 387, 390
 - dorsalis (of turtles), 387
 - geniculatus (of reptiles), 385–386, 388–389
 - gray (of anurans), 375, 377
 - of hagfishes, 375, 378
 - medial (of mammals), 380, 384, 386–387, 394, 396
 - olivary (of mammals), 380, 384–385, 387, 394–396
- periventricular:
 - of cartilaginous fishes, 291, 374, 378, 392
 - dorsal:
 - of non-teleost ray-finned fishes, 375
 - of teleosts, 378–379, 393
 - ventral:
 - of non-teleost ray-finned fishes, 375–376
 - of teleosts, 378–379, 393
- posterior, of:
 - gars and bowfin, 375–376
 - mammals, 380, 384–388, 394, 396, 480
 - teleosts, 375–376, 379–383, 453, 658
- of ray-finned fishes, 281
- superficial:
 - of cartilaginous fishes, 374, 378
 - intermediate (of teleosts), 380–381, 383, 392, 453, 658
 - magnocellular, of:
 - gars and bowfin, 375–376
 - teleosts, 324, 379–383, 392–393, 399
 - parvocellular, of:
 - gars and bowfin, 375–376
 - reedfishes and sturgeons, 375
 - teleosts, 379–383, 392–393
 - ventral (of reptiles), 385, 387, 389
- pretrigeminal, 582–583
- principalis precommissuralis (of birds), 390–391
- principal, of torus semicircularis (of amphibians), 576
- profundus mesencephali, of:
 - amphibians, 294, 321
 - birds, 268
 - reptiles, 301
- pulvinar (of mammals), *see* Nucleus, lateral(is), posterior/pulvinar complex
- putamen, *see* Nucleus, caudate-putamen
- of the raphe:
 - centralis superior, 227
 - dorsalis, 299
 - general aspects, 134, 222, 224–226, 229–230, 232, 234, 236, 249, 255, 268–269, 272, 275–277, 280, 300, 392, 395, 407, 411–412, 432, 455, 460, 474, 480, 550, 612, 622, 626, 629, 655
 - inferior, 323, 380–381
 - magnus, 551
 - medial, 299

- pallidus,
superior, 276, 279, 295, 454, 456, 473
- red:
of amphibians, 290, 292, 294
of birds, 262, 290, 292, 302, 564, 566
of cartilaginous fishes, 279, 290–294, 296–297, 322
general aspects, 151, 242, 256, 269, 272–273, 289–294,
296–299, 301–302
of lungfishes, 277, 290, 292–293
of mammals, 261, 269, 273, 281, 290, 292–293, 299, 384,
425
of ray-finned fishes, 290, 292, 298
of reptiles, 262, 290, 292, 301
- reticular(is):
caloris, 187, 328
dorsalis, 224, 228–231
dorsolateral (of hagfishes), 279, 295
gigantocellularis, 224–226, 228–231, 233–234, 236
inferior, 224–225
isthmus group, 225
lateralis, 224, 228, 230–231, 550
magnocellularis, 224, 226, 228–231, 233–234, 236
medial (of ray-finned fishes), 276, 280
medius, 224–225
mesencephali, 224–225, 229, 236
paragigantocellularis, 224, 226, 229–231, 550
paramedianus, 228, 230–231
parvocellularis, 224, 226, 228–231, 234, 236
pedunculopontinus, *see* Nucleus, pedunculopontine
pontis:
caudalis, 224, 226, 228–230, 236
oralis, 224, 226–230, 234, 236, 271
retroambiguus, 589
rhombencephalic:
anterior, 223
middle, 223
posterior, 223
subcoeruleus, 224, 226–230, 232
subthalamic, of mammals (including the nucleus of Field H
of Forel), 478
superficial isthmal (of frogs), 294, 474, 476
superior:
pars dorsalis (thalamic reticular nucleus) (of birds), 352
of lampreys, 225
tegmenti pontis, 224
thalamic:
of birds, *see* Nucleus, reticular(is), superior, pars
dorsalis
of crocodiles, 352
general aspects, 228, 230
of mammals, 234, 352, 355, 424–425, 478
trigeminal group, 225
ventralis, 224, 226, 228–231
ventromedial (of hagfishes), 279, 295
- retrobulbar, 233
- reuniens:
of mammals, *see* Nucleus, medioventral
pars compacta (of reptiles), *see* Nucleus, medial(is), of
lizards
pars diffusa (of reptiles), 431–432, 437, 508–509, 562, 576
- rhomboidal, 430, 436
- robustus, *see* Arcopallium, nucleus, robustus arcopallii
- rostral:
entopeduncular, *see* Nucleus, anterior, entopeduncular
vestibular (of birds), 200
- rostrrolateralis, 12, 413–414
- rotundus:
of birds, 330, 332–333, 335, 387, 390–391, 395, 428,
431–432, 437, 508–509, 538, 562
general aspects, 335, 395, 508–509
of reptiles, 329, 335, 395, 419, 427, 431–432, 437,
508–509, 538, 540
- ruber, *see* Nucleus, red
- sacci vasculosi, 446
- salivatory:
inferior, 206, 209–211
superior, 206, 209–211, 215
- secondary:
gustatory, *see* Nucleus, gustatory, secondary
isthmal, 455
of octaval column, 212
visceral, 455
- semilunaris:
of birds (in isthmal region), 330
parovoidalis (of birds), 431–432, 437, 508–509, 562–563
- septal, *see* Septum
- septoformal, of septum, *see* Septum, nucleus, septoformal
- solitarius, 178, 184, 190–191, 233, 256, 456, 487
- sonic motor, 211
- sphericus, *see* Amygdala, nucleus sphericus
- spinal accessory, *see* Nucleus, accessory spinal
- spinal cord electromotor relay, 213
- spinotrigeminal funicular (of teleosts), 193–194
- spiriformis lateralis, *see* Nucleus, lateral spiriform
- spiriformis medialis, *see* Nucleus, medial spiriform
- stria terminalis, bed, *see* Nucleus, bed, of, stria terminalis
- subcuneiformis, 228–230
- subelectrosensorius, 298
- subeminentialis pars magnocellularis, 258, 325
- subglomerulosus, 399
- subhabenular:
of birds, 431, 437
of hagfishes, 418, 422
- subhippocampal thalamic (of lampreys), 407–408
- subparafascicular, 430–431
- subpretectalis (of birds), 302, 387, 390, 395
- substantia:
innominata, *see* Substantia innominata
nigra, *see* Substantia nigra
- subthalamic:
of birds, 390, 479, 485–487
of mammals (corpus Luysii), 284, 300, 303, 425,
478–485
of reptiles (anterior entopeduncular nucleus), 479, 484
reticular (of mammals), *see* Nucleus, reticular(is),
subthalamic
- subvalvularis, 258, 325
- superficial(is):
basalis (of cartilaginous fishes), *see* Area, superficialis
basalis
isthmal/ic (of *Latimeria* and lungfishes), 277, 281, 293
parvocellularis, of OPT complex (of birds), *see* Nucleus,
dorsal(is), lateral geniculate, of birds
- superior:
olivary:
general aspects, 198–199, 214, 305, 574–576
lateral, 577
medial, 574, 577
salivatory, *see* Nucleus, salivatory, superior
vestibular (of anurans and mammals), 198, 200
- suprachiasmatic, of preoptic area/hypothalamus, *see*
Hypothalamus, nucleus, suprachiasmatic

- supracommissural, of ventral telencephalic area (of ray-finned fishes), *see* Area, ventral(is), telencephalic, nuclei of, supracommissural (Vs)
- suprageniculate (of mammals), *see* Nucleus, limitans/suprageniculate
- supramammillary (of mammals), 622
- supraoptic, of hypothalamus, *see* Hypothalamus, nucleus, supraoptic
- supraspinal (of birds), 209, 230
- taeniae, *see* Amygdala, nucleus, taeniae, amygdalae
- tangential vestibular (of birds), 200
- tectal gray (of turtles), 386
- tegmenti pedunculopontinus, 268, 271–272
- tegmento-olfactorius, 605
- term, 55
- thalamic reticular, *see* Nucleus, reticular(is), thalami
- triangularis (of birds), 428, 431–432, 509, 540
- triangular, of septum, *see* Septum, nucleus, triangular
- trigeminal:
- descending, 177, 184–187, 194, 210, 429, 435–436, 438, 549, 561
 - general aspects, 548, 550
 - lateral (of snakes), 187
 - mesencephalic (of jawed vertebrates), 185–186, 210, 269–270, 273, 279, 281, 289–291, 296, 298–299, 322
 - motor, 186, 206, 208, 210, 227, 247, 277, 279, 281, 295, 501, 559, 582, 587–589
 - principal sensory, 177, 184–185, 256, 281, 321–322, 429, 435–436, 438, 549, 556–557, 563
 - of the telencephalon in birds, *see* Nidopallium, nucleus, basorostralis pallii (Bas)
- trochlear, 206–207, 210, 216, 234, 236, 269–272, 276, 294, 380–381, 391–393
- tuberculohabenular (of trout), 410
- uvulaeformis, 584
- ventral(is):
- accessory optic, of:
 - bowfin, 376
 - cartilaginous fishes, 279
 - teleosts, 379, 392–393
 - anterior, 300, 424–425, 429, 435, 438, 479–485, 549, 565
 - of area acousticolateralis, 197
 - lateral geniculate (of amniotes), 350–351, 384, 390–391, 425, 436, 531
 - lateral(is), 261, 424–425, 429, 435–436, 438, 480–485, 549, 558–560, 565
 - medullary (of teleosts), 211–212
 - of octaval column, 197
 - posterior inferior (of mammals), 425, 429
 - posterolateral(is):
 - of mammals, 424–425, 435–436, 507–508, 548–549
 - pars caudalis, 429, 549–550, 552
 - pars oralis, 429, 549, 558–560, 565
 - posteromedial(is), 424–425, 435, 548, 550, 552, 556–557, 561
 - tegmental (of hagfishes), 294–295
 - tuberis, 212
 - of ventral telencephalic area (of ray-finned fishes), *see* Area, ventral(is), telencephalon, nuclei of, ventral (Vv)
- ventrolateral(is):
- of amphibians, 350, 433
 - of fishes, 350
 - of nonmammalian amniotes, 351
 - parabrachial (of birds), 589
 - of rostral medulla (of birds), 589
 - tegmental, 322
 - ventrolateral vestibular (of nonmammalian amniotes), 198, 200
 - ventromedial(is), of:
 - amphibians, 433
 - fishes, 350
 - nonmammalian amniotes, 198
 - ventromedial vestibular (of reptiles), 200
 - vestibular, 150–151, 179, 184, 236, 254, 262, 322, 385–386, 391, 394–395
- X, of:
- mammals, 549, 558–560
 - sharks, *see* Nucleus, A
 - zona incerta (of mammals), *see* Zona, incerta
- Obex, 135
- Oblique, term, 667–668
- Ocellus, *see* Eye(s), ocelli/us
- Octopuses, *see* Mollusca/s, cephalopods
- Oil droplets, retinal, 35
- Olfactory:
- accessory bulb, 41, 181, 487, 593–595, 601, 603–605
 - cortex, *see* Cortex, olfactory
 - epithelium, *see* Epithelium, olfactory
 - general aspects of system, 39–41, 118, 353, 359, 593–605, 611
 - glomerulus, 593, 595, 597, 600
 - macrosmatic, 367
 - main bulb:
 - general aspects, 39, 41, 44, 64, 66–67, 99, 180–181, 232, 268–269, 312, 344, 356–357, 362–363, 367, 408, 430, 451, 488, 495, 497, 500, 503, 510, 593, 595, 597, 601, 603–605, 611–613, 616
 - layers of, 594–601
 - mucosa, 41
 - nerve, *see* Nerve, cranial, olfactory
 - pallium, *see* Pallium, olfactory
 - receptor cells, *see* Receptors, olfactory system
 - tract, *see* Tract, olfactory
 - tubercle, *see* Tubercle, olfactory
- Olszewski, J., 224
- Opening, *see* Fenestra
- Opioids, 552
- Opisthocentrus*, 254
- Opitz, J., 7
- Opossums, 98, 249, 254, 505, 531–532, 555, 557, 559–560
- Optic:
- chiasm, *see* Chiasm, optic
 - tectum, *see* Tectum, optic
- Optokinetic nystagmus, 391
- Oral, term, 665–667
- Orangutan, 83, 105
- Orbit(s), 80, 82, 169, 525–526
- Order, term, 3
- Oreochromis*, 380
- Orexin, 235, 448
- Organization:
- columnar, 104, 355, 533, 535, 539, 543, 577–578, 580
 - elaborated, term, 85, 87–89
 - isomorphic, 44–45
 - laminar:
 - of nuclei, 526–531, 577
 - term, 84, 86, 88–89
 - multiple representations, 547, 556–559, 566, 577

- neuromeric, 53, 164–166, 657
 retinotopic, *see also* Organization, topographic. 43–44, 533, 539, 543
 segmental, *see also* Segment. 147
 somatotopic, 43–45, 148–149, 255, 547–548, 552–557, 560–561
 tonotopic, 43–44, 574, 581, 588
 topographic, 43–47, 258, 312, 315–316, 319–320, 322–323, 325–326, 334, 355, 361, 385, 427, 436, 547, 558, 560–561, 574, 577–579, 655
 visuotopic, *see* Organization, retinotopic
- Organ(s):
 ampullary, *see* Receptors, electrosensory, ampullary
 balance (of *Branchiostoma*), 647–648
 circumventricular, 145, 448–450, 460
 of Corti, 32
 Eimer's, *see* Receptor(s), mechanosensory, Eimer's organs
 electric, 41, 144, 195, 212–213, 221, 259, 501
 frontal:
 of amphibians, 407, 409, 414
 of *Branchiostoma* (frontal eye), 647–649
 of Jacobson, *see* Organ, vomeronasal
 lateral line, 33–34
 palatal, 39, 192–193
 parapineal, 407, 409, 413–414
 paratympanic, 200
 periventricular (of amphibians), 454
 pineal, *see* Pineal (eye/gland/organ)
 pit, 30, 34, 37
 rostral (of *Latimeria*), 195
 Schreiner, 188
 sensory (of ascidian), 646
 spiracular, 195, 200
 subcommissural, 145, 296–297, 351, 374, 376, 388–389
 subfornical, 448
 tendon, 31
 tuberos, *see* Receptors, electrosensory, tuberos
 vestibular, 30
 vomeronasal, of Jacobson, 39–41, 181, 603
- Orientation, terms, 61, 665–667
- Orthogenesis, 116–117
- Oryzias*, 650
- Ostariophysans, *see also individual common name and genus listings*. 305, 380–381, 397–398, 499, 615
- Osteichthyes, term, *see also* Actinopterygians. 74
- Osteoglossomorpha/s, *see also* Mormyrids and Notopterids. 76, 78, 96, 245, 305, 380, 382–383, 397, 413
- Osteoglossum*, 380, 382–383
- Ostracoderms, 414
- Otters, 94, 137, 208
- Out-group, 14–15
- Outside-in, in development of nuclei, 57, 658
- Ovary, 447, 449–450, 453
- Oviduct, 447, 453, 461
- Owen, R., 8
- Owls, 152, 516, 540–541, 543, 560, 573–574
- Oxytocin, 26
- Oysters, *see* Mollusca/s, bivalves
- Paddlefishes, *see* Chondrostei
- Paleostriatum:
 augmentatum, of:
 birds, *see* Striatum laterale
 turtles, *see* Striatum, dorsal, of reptiles, of turtles
 primitivum, (of birds), *see* Pallidum, dorsal, of birds
 ventral (ventral pallidum), *see* Pallidum, ventral(e), of birds
- Pallidum:
 dorsal (globus pallidus):
 of anamniotes, 354, 472–477, 603
 of birds, 345, 363, 368–369, 485–488, 540, 543, 565
 general aspects, 297, 365–367, 471–472, 474, 477, 480–483, 512
 of mammals, 297, 300, 328, 350, 355, 359–360, 365, 367–369, 385–388, 395–396, 411, 429, 435–437, 471, 477–483
 of reptiles, 328, 368–369, 484
 general aspects, 60, 66, 68, 352, 362
 ventral(e):
 of anamniotes, 354, 473–475, 603
 of birds, 345, 363, 368, 484–485, 487
 general aspects, 297, 365–367, 471–472
 of mammals, 300, 365–367, 471, 478, 482–483, 487
 of reptiles, 368, 484, 604
- Pallium:
 central nucleus (of sharks), 354, 418, 434, 498, 655
 divisions:
 collopallium, 120, 361, 495, 509, 511, 656–657
 lemnopallium, 120, 361, 499, 501, 507, 510–511, 656
 dorsal, 343, 352–354, 361, 418, 437–438, 495–499, 501, 510, 548, 566, 606, 594–595, 611, 613, 656–657
 dorsolateral, of cladistians, 353, 496, 500, 595, 612–613
 dorsomedial:
 of cladistians, 353, 496, 500, 595–596
 of *Latimeria*, 497, 597
 general aspects, 66, 69, 343–344, 352–353, 489, 495–499, 512
 hippocampal, *see* Hippocampus, pallium
 lateral, 343, 352–354, 361, 408, 418, 427, 435, 495–498, 512, 594–595, 597–598, 603, 606, 612–613, 653, 655–657
 limbic, 495
 medial, 343, 352–354, 361, 363, 369, 396, 408, 418, 432–435, 437, 453, 495–499, 512, 575, 594–595, 611–615, 623, 625–627, 630, 653, 655–656
 olfactory, 594–595, 598, 653
 P1 (of cladistians), *see* Pallium, dorsomedial, of cladistians
 P1–P5 (of hagfishes), 353–354, 422, 498, 597–598, 615
 P2–P3 (of cladistians), *see* Pallium, dorsolateral, of cladistians
 piriform, *see* Pallium, olfactory
 thickening, 343, 362, 436, 507, 564, 580
 ventral, 120, 343, 353, 361, 495, 497–498, 512, 656–657
 ventromedial (of *Latimeria*), 497, 597
 visual, 536
- Pan*, *see* Chimpanzees
- Pantodon*, 380, 382, 397, 413
- Papez, J., 622–623
- Papilla:
 amphibian, 575
 basilar, 32, 43, 573, 575–576
 gustatory, 38
- Parallelism, 9, 12–13
- Parasagittal, term, 666–667
- Parasympathetic nervous system, *see* Autonomic nervous system, parasympathetic division
- Parcellation, *see* Evolution/ary, mechanisms, parcellation and Theory, parcellation
- Parietal eye, *see* Eye, epiphyseal
- Parkinson's disease, 296–297, 303
- Parrots, 85, 102, 152, 515–516, 583, 585
- Parsimony, 14–15
- Pastor, A., 216
- Patches, of dorsal striatum (of rats), 479, 484

- Path, perforant, *see* Tract, perforant path
- Pathway(s), *see also* Bundle(s) and Tract(s/us).
- dopaminergic, 233
 - dorsal column, *see* Column, dorsal
 - efferent cochlear, *see* Bundle, olivocochlear
 - electromotor, 212–213, 658
 - GABAergic, 234
 - hypophyseal:
 - anterior, 460
 - posterior, 460
 - lemniscal, 131
 - mesolimbic, 233
 - neospinothalamic, term, 553
 - noradrenergic, 232–233
 - paleospinothalamic, term, 553
 - respiratory, 582–585, 588
 - vocal:
 - control, 211–212, 575, 582–588, 658
 - learning, 95
- Patterson, C., 15
- Peduncle:
- cerebellar:
 - inferior (restiform body and juxtarestiform body), 242, 255
 - middle (brachium pontis), 242, 255
 - superior (brachium conjunctivum), 242, 261–262
 - cerebral, term, 289
 - mammillary, 460
 - olfactory, 594
- Pelecanus*, 217
- Penguins, 138, 208
- Pepperberg, I., 516
- Peptides, 25
- Perientopallium, 540–541, 565
- Pes pedunculi, 269, 289, 299, 361, 384, 424–425
- Petras, J., 118
- Petromyzon*, 75, 270, 276, 290, 316
- Petromyzontida/formes, term, *see also* Lampreys. 74
- Petrovich, G. D., 119, 359, 657
- Pettigrew, J. D., 188, 560
- Phalacrocorax*, 217
- Phalanger, 566
- Pharynx, 582
- Pheromones, 39, 41, 603, 605
- Phillips, J. B., 313
- Pholidapus*, 254
- Photopigments, 35
- Photoreceptors, *see* Receptors, light
- Phyletic:
- continuity, 8
 - evolution, term, *see also* Evolution, phyletic. 6
 - studies, 93, 109
- Phylogenetic:
- progression, *see also* Phyletic, evolution. 116
 - scale, *see* *Scala Naturae*
 - tree, 95–97
- Phylogenetic(s)/Phylogeny, 93, 95–97
- Phylum, term, 3
- Pigeons, *see also* *Columba*. 88, 94–95, 102, 147–148, 152, 211, 244, 261, 282, 284, 302, 329, 331–332, 363, 390–391, 394, 428, 456, 459–460, 485, 502, 511, 513–515, 541, 562, 579, 581
- Pigs, 98, 105, 184, 303, 553
- Pikaia*, 650, 652
- Pineal (eye/gland/organ), *see also* Epiphysis. 66, 269, 345, 407–409, 414
- Pineal/parapineal complex, 407, 409, 414, 649, 652–653, 655
- Pinkus, T., 69
- Piriform, term, 353
- Pit, sensory, *see* Receptor, infrared
- Pituitary, *see* Hypophysis, Adenohypophysis, and Neurohypophysis
- Placoderms, 414
- Placode(s):
- adenohypophyseal, 168
 - dorsolateral:
 - general aspects, 135–136, 163, 167
 - octaval, 163
 - postotic, 167
 - preotic, 167
 - epibranchial, *see* Placode(s), ventrolateral
 - general aspects, 54, 61, 158, 161–170, 174–175, 644, 649, 651–653, 657–658
 - glossopharyngeal, 164
 - hyoid, 164
 - lens, 163–164
 - nasal, 164
 - olfactory, 167–168
 - profundus, 163–164, 167–168
 - trigeminal, 163, 167
 - vagal, 164
 - ventrolateral, 163, 167
- Planaria*, *see also* Platyhelminthes. 638–639, 642
- Planes of section, 27, 61, 666–668
- Plate:
- alar, 54–55, 176
 - basal, 54–55, 176
 - cortical, 56
 - floor, 54–55
 - prechordal, 650
 - preplate, *see* Preplate
 - roof, 54–55
 - subplate, *see* Subplate
 - ventral cell (of snakes), 623, 625
- Platyhelminthes (including *Planaria*), 638–639, 641–642
- Platypuses, 41, 83, 152, 188, 234, 505, 554–555, 561
- Platyrrhinoidis*, 423
- Plesiomorphic/y, 13–14, 16
- Plesiosaurs, 102
- Plethodon*, 433, 613
- Plethodontidae, 104
- Plexus, marginal dendritic, 140–141
- Podarcis*, 434, 627
- Poling, L. L., 82
- Polypterus*, 353, 473–474, 477, 496, 500, 613
- Pons, *see* Hindbrain
- Porichthys* (plainfin midshipman), 211–212, 420
- Porpoises, 102, 138, 208, 237, 249
- Posterior:
- term, 665–667
 - tuberculum, *see* Tuberculum, posterior
- Posture, 667
- Potential(s):
- action, 30
 - graded, 30
 - excitatory postsynaptic, 24
 - inhibitory postsynaptic, 24
 - local, 30
 - muscle action, 144
 - receptor, 30, 32
 - resting, 24, 30

- Predation, *see* Behavior, predatory
- Preglomerular nuclear complex:
 - of gars and bowfin, 292, 376, 396
 - general aspects, 193–194, 196, 292, 344, 349–350, 396, 439, 499, 501, 653, 655
 - of teleosts, 193–194, 196, 382–383, 396–399, 454, 611
- Preplate, 56
- Pretectum, *see also* Nuclei, pretectal(is).
 - of amphibians, 375, 377
 - of birds, 385, 387–389
 - of cartilaginous fishes, 374, 378, 408
 - general aspects, 65, 68–69, 269, 320–321, 343–344, 349, 351, 373–389, 398, 408–410, 476, 478, 480, 548, 612, 655, 657–658
 - of hagfishes, 375, 378
 - of lampreys, 374
 - of lungfishes, 456
 - of mammals, 232, 269, 380, 384–386, 548
 - of ray-finned fishes, 256, 258, 375–376, 378–383, 398, 423
 - of reptiles, 385–389, 450
- Primates, 96, 137, 147, 152, 228, 249, 301, 303, 325–326, 344, 350, 356–358, 361, 410, 420, 429–430, 435, 478–479, 501, 503–507, 514–515, 536, 548, 551, 553, 555–559, 603, 606, 619, 621, 623, 629
- Principle:
 - auxiliary, of Hennig, 9
 - of minimum increase in complexity, 14
 - of parsimony, *see* Parsimony
 - of proper mass, 109
- Prionotus*, 38, 398
- Pritz, M. B., 118–119
- Proctodeum, 51
- Procyon*, 281, 299, 424–425, 531
- Prolactin, 25
- Prosencephalon, *see* Forebrain
- Prosimians, 528, 534, 556, 566
- Prosomere, 53
- Protein, argyrophilic NOR-associated, 617
- Protocerebrum, 639–641, 645
- Proto-DVR, *see* Dorsal, ventricular ridge, proto-DVR
- Protopterus*, 79, 277, 293, 475, 497, 614
- Protostoma/es, 637–639, 641, 643–645
- Protosuchus*, 33–34
- Prototheria, term, *see also* Monotremes. 80, 83
- Protovertebrae, 651–652
- Protovertebrate, 650
- Proximal, term, 666
- Pseudemys*, 362, 484
- Pseudolayers (of Wulst in birds), 510–511
- Pterobranchs, *see* Hemichordates
- Puelles, L., 120, 417, 657, 512
- Puffer fish, 140
- Pulvinar, *see* Nucleus, lateral(is), posterior/pulvinar complex
- Punctuated equilibrium, 6
- Purkinje, J., 246
- Putamen, *see* Nucleus, caudate-putamen
- Quadrupeds, *see* Tetrapods
- Rabbits, 83–84, 97–98, 152, 303, 356, 526, 531–532, 555, 560
- Rabl-Rückhard, H, 69
- Raccoons, *see also* *Procyon*. 137, 147, 281, 531, 553, 559–560, 566
- Radiant energy:
 - infrared, 30–31, 37
 - ultraviolet (UV), 30–31
 - visible light, 31, 34–35
- Radinsky, L., 94
- Raff, R., 7
- Ragsdale, C. W., 510
- Raja*, 77, 88, 151, 279, 296–297, 322, 378, 476, 615
- Ramon-Moliner, E., 23, 116, 223
- Ramón, P., 69
- Ramón y Cajal, S., 69
- Rana*, 79, 278, 304, 320, 349–350, 354, 377, 418, 422, 475, 497, 575, 582–583, 614
- Raphe, *see* Nucleus, of the raphe
- Ratfishes, 73, 75–77, 86, 88, 247, 275–276, 293, 303, 316
- Rats, *see* Rodents
- Rattus*, *see also* Rodents. 408
- Ray-finned fishes, *see* Actinopterygians
- Rays, 76, 89, 95, 284
- Rays, nasal (of star-nosed mole), 33, 44–46, 556–557
- Recapitulation, von Baerian, *see* von Baerian recapitulation
- Receptive field, 32, 46
- Receptor(s):
 - and adaptation, 30, 32
 - and awareness, 29–30
 - chemoreceptors, solitary, 38, 188
 - chemosensory, 31, 37–41
 - classification, 31
 - dome pressure, 33–34
 - electrosensory:
 - ampullary organs, 31, 42–43, 179, 259
 - general aspects, 19, 31, 41–42, 134, 179, 259, 262, 555
 - knollenorgan, 259
 - of monotremes, 179, 188, 555
 - mormyromasts, 259
 - tuberos organs, 31, 42–43, 179
 - exteroceptors, 29
 - free nerve endings, 31
 - general aspects, 20–21, 28–29
 - general chemical, 31
 - gustatory, 31, 37–40, 189–190
 - hair:
 - cell, 31, 32
 - follicle, 32, 548
 - hearing, 31
 - infrared, 31, 37, 185, 187
 - interoceptors, 29
 - joint, 31, 548
 - lamellar body, *see* Body, lamellar
 - lateral line, 31, 33–34
 - light:
 - cones, 31, 35–36
 - general aspects, 31, 450
 - of median eye, 37
 - rods, 35–36
 - magnetosensory, 31, 34, 188
 - mechanosensory:
 - adaptation, 32
 - Eimer's organs, 33
 - general aspects, 31–32, 139, 313, 555
 - of monotremes, 188, 555
 - neuromasts, 33, 179
 - vibrissae, 556
 - muscle, 31, 548
 - nociceptive, *see* Receptors, pain
 - ocellus, *see* Eye(s), ocellus/i
 - olfactory, 31, 39–41, 593–594, 597–598, 600
 - pain, 31, 42–43, 139

- pit organ, *see* Organ(s), pit
 potential, 30–31
 pressure, 139
 radiant energy, *see also* Radiant energy. 31, 34–37
 Ruffini endings, 31
 skin:
 rapidly adapting, 31, 548
 slowly adapting, 31, 548
 statocyst, *see* Statocyst
 stretch, 21, 31
 taste buds, *see* Receptor(s), gustatory
 temperature, 31
 touch, 31, 33, 139, 548–549
 ultraviolet, 31
 vomeronasal, 39–41
 Redies, C., 542
 Reedfishes, *see* Cladistia and Polypteru
 Reelin, 56, 656, 658
 Reflex(es):
 acoustic, 207, 213–214
 arc, 132
 dorsal light, 258, 374
 excitatory, 131
 general aspects,
 inhibitory, 131
 monosynaptic, 131–132
 optokinetic, *see also* Optokinetic nystagmus. 394
 patellar, 132
 polysynaptic, 132
 pupillary light (pupillary constriction), 375, 385
 Region(s):
 midbrain locomotor, *see* Midbrain locomotor region
 tuberal, *see* Adenohypophysis, pars tuberalis
 Reichert, H., 641
 Reiner, A., 70, 119–120, 333, 437, 510–512, 565
 Reissner, *see* Fiber(s), Reissner's
 Reptiles, *see also* Crocodiles, Lizards, Snakes, Turtles, and
 Sphenodon. 80, 82, 88, 101, 103, 119–120,
 131, 135, 187, 190, 205, 283, 290, 301, 303,
 305–306, 312–313, 327–333, 335, 344, 350–351,
 361–364, 368–369, 380, 385–389, 394–396, 407,
 409, 412, 414, 419–420, 426–427, 431–432, 434,
 436–439, 446–447, 479–480, 483–485, 488–489,
 502, 504, 507–511, 538, 576, 579, 581,
 583–588, 601, 603, 605, 617, 623–630, 655–658
 Resemblance, minuteness of, 9
 Respiration, 133
 Reticular formation, *see also* Nucleus, reticularis.
 A cell groups of Dahlström and Fuxe, *see* Cell groups, A
 adrenergic pathway, 232
 ascending, 221
 B cell groups of Dahlström and Fuxe, *see* Cell groups, B
 descending, 221
 dopaminergic, 233
 evolution, *see* Evolution, of reticular formation
 functions, 221, 234–236
 general aspects, 64, 69, 131, 133–135, 210–211, 218,
 221–237, 247, 256, 261, 267–269, 272, 275,
 281, 284, 304, 314–315, 317–318, 321–323, 326,
 329–330, 352, 374, 385–386, 394, 407, 411–412,
 430, 435, 474, 476, 483, 501, 511, 552,
 559–561, 564, 566, 583, 587, 605, 612, 626, 655
 gigantocellular, 222
 isthmus group, 225
 lateral, 151
 magnocellular, 222
 medial, 151, 249, 280
 medial nucleus of, 276
 nomenclature, 224
 nucleus reticularis thalami, *see* Nucleus, reticularis, thalami
 organization, 222–230
 parvocellular, 222
 pathways, 230–236
 of pons, 281
 and sleep, 234–236
 superficial isthmal (of amphibians), 294
 superior (of birds), *see* Nucleus, reticular(is), superior, pars
 dorsalis
 trigeminal group, 225
 Retina:
 cells:
 amacrine, 35–36
 bipolar, 35–36, 529–531
 bistratified, 529
 cones, *see* Receptors, light, cones
 ganglion:
 displaced, 394
 of ganglion cell layer, 394
 horizontal, 35–36
 parasol, 529
 P (X, parvocellular), M (Y, magnocellular), and K
 (W, koniocellular), 529–531, 534–535
 rods, *see* Receptors, light, rods
 general aspects, 35, 451, 455, 527–528, 530–531, 537, 543,
 578, 605
 layers, 35–36
 Reversals, 9, 11–13
 Rexed, B., 147
 Rhombencephalon, *see* Hindbrain
 Rhomboid sinus, *see* Sinus, lumbosacral
 Rhombomere(s), 53, 164, 167, 640–641
 Rhynchocephalia, term, *see also* *Sphenodon*. 79–80
 Rhythms, biological, 346, 407–409, 445–451, 460
 Ridge:
 dorsal granular (of cerebellum), 248
 dorsal ventricular, *see* Dorsal, ventricular ridge
 lateral granular (of cerebellum), 248
 Rioch, D., 119
 Rockling, 38
 Rodents, *see also* Ground squirrels; Hamsters; Mole rats, blind;
 and Squirrels. 44, 83, 96–98, 105, 152, 230–231,
 248–251, 254, 268–269, 301, 303, 344, 351,
 355, 360, 366–367, 385, 408, 448, 477, 479,
 502–503, 511, 526, 531–532, 554, 556, 559–560,
 566, 603, 619–620, 639–642, 650
 Rodríguez, E., 499, 616
 Rods, *see* Receptors, light
 Romer, A. S., 136
 Ronan, M. C., 118
 Ropefishes, *see* Cladistia
 Rose, J., 543
 Rose, M., 69, 580
 Rosette (of cerebellar cortex), 255
 Rostral, term, 61, 665–667
 Roth, G., 433
 Röthig, P., 69
 Roth, L. V., 12
 Rubenstein, J. L. R., 120, 657
 Ryugo, D., 258
 Saccade, 324, 326, 391
 Saccus vasculosus, 446
 Sac, vocal, 582
 Sagittal, term, 666

- Saidel, W. M., 12, 413
 Saiga, H., 646
Saimiri, *see* Monkeys, squirrel
 Salamanders, *see* Urodela/es
Salamandra, 319
 Salamandridae, 104
 Salas, C., 216, 499, 501, 616
Salmo, 380, 382, 500, 599
 Sanides, F., 115
 Sarcopterygians, *see also* Crossopterygian, Lungfishes,
and Tetrapods. 73–74, 76, 84, 86–88, 96,
 137
 Sasai, Y., 641
 Saunders, P. T., 14
Scala naturae (phylogenetic scale), 4, 60, 95–97, 101, 104,
 107–108, 113, 116–117, 553
 Scale, phylogenetic, *see* *Scala naturae*
 Scandentia, 528
Scapbhirhynchus, 197, 500
 Schroeder, D. M., 119
 Sclera, 35
Scyliorhinus, 323
 Sea:
 robin, 38
 squirts, *see* Urochordata/es
 urchins, *see* Echinodermata/s
 Seals, 138, 208, 237, 303
Sebecus, 33–34
 Second messengers, 25
 Segment, head, *see* Head, segmental organization
 Senses, *see also* Receptors.
 audition, 33, 135
 electrosensory, 31, 41–42, 134–135, 144, 311,
 555
 general aspects, 28–30
 gustation (taste), 31, 37–40, 131, 135
 infrared, 31, 37, 311–312, 328
 lateral line, 31, 33–35, 135
 magnetic, 188, 311, 313
 mechanoreception, 31–33, 135
 olfaction (smell), 31, 39–41, 168
 pain:
 fast, 553
 general aspects, 31, 42–43, 134, 236, 548–553
 slow, 552–553
 pressure, dome, 33–34
 somesthesia, 135, 550, 563
 temperature, 134
 touch, 31, 134
 vestibular, 31–32, 141, 151
 vision (light), 31, 35–37, 168
 Sensory:
 pit, *see* Pit, sensory *and* Receptor, infrared
 transduction, 30
 Septum/Septal area:
 area, of hagfishes, 628
 general aspects, 60, 66, 232–233, 343, 352, 354, 359, 362,
 364–365, 369, 409–411, 433, 450–451, 456–457,
 460, 471, 477, 512, 564–565, 595, 603–605,
 611, 628, 630
 lateral and medial nuclei, of:
 anamniotes, 474–475, 489, 612–615, 628–629
 birds, 345, 369, 511, 629
 mammals, 354, 366–368, 488–489, 499, 616, 618–619,
 621–623, 626, 629
 reptiles, 368–369, 624–626
 of lungfishes, *see* Subpallium, medial
 nucleus:
 of the diagonal band of Broca, 345, 354, 365–369, 409,
 411, 488–489, 595, 612–614, 628–629
 septofimbrial (of mammals), 369, 411, 629
 triangular (of mammals), 369, 411, 629
 of ray-finned fishes, *see* Area, ventral(is), telencephalon, nuclei
 of, ventral (Vv)
 Serotonin (5-HT), 25, 142, 230, 232, 235, 268, 275, 277, 281, 436,
 460, 471–474, 477, 480, 552, 612, 622, 626, 655
 Sexual dimorphism, 151, 450, 457, 585–586
 Shanklin, W. M., 69
 Sharks, *see* Chondrichthyans
 Sheep, 137, 249–250, 560, 619
 Sheldon, R. E., 69
 Shelf, *see* HVC, shelf
 Shettleworth, S. J., 628
 Shimizu, T., 542
 Shrews, 33, 98, 105, 303
 Silurids, *see* Catfishes
 Simeone, A., 641
 Similarity:
 multiplicity of, 9
 term, 8
 Simpson, G. G., 8–9, 117
 Sinus, lumbosacral, 146–147
 Sirenians, 237
 Skates, 76–77, 88–89, 275, 279, 284, 296–297, 322, 324, 378,
 418, 423, 476, 499, 598, 601, 613, 615
 Skin (glabrous and hairy), 449, 548, 557
 Skull:
 evolution, *see* Evolution/ary, of skull
 structure, 159–160
 Sleep, *see also* Wakefulness.
 dreaming, 221
 fast-wave, 234, 236
 general aspects, 221, 234, 236, 352, 448
 monocular, 237
 REM (rapid eye movement), 234, 236
 slow-wave, 230, 234, 236
 unihemispheric, 237
 Smith-Fernandez, A., 120
 Smith, H. M., 9–11
 Snails, *see* Gastropoda/s
 Snakes, 146–147, 187, 290, 292, 301, 303, 312, 328, 362, 409,
 436, 457, 576, 601, 603–604, 623, 625
 Snout, 555–556, 561
 Soares, D., 33–34
 Soma, 20, 21
 Somatostatin, 25, 449, 462, 471–472, 476, 552, 586
 Somite(s), 52, 55, 159, 161–164, 167–168, 170, 649
 Somitomere(s), 159, 161–170, 649
 Sonic motor system, 211
 Sound localization, 571–574
 Space, subarachnoid, 66
 Special, word, 3
 Speciation, *see* Cladogenesis
 Species:
 sister, 6
 term, 3
 Speech, *see* Language
Spheniscus, 217
Sphenodon (tuatara), 79–82, 86, 96, 409, 414, 603, 606
 Sphincter:
 anal, 463
 urinary, 461
 Spinal cord:
 autonomy, 133

- cervical, 63, 539, 559–560, 564, 566
 coccygeal, 560
 columns, 128–129, 139
 dorsal horn, 130, 140, 145, 148, 150, 236, 549–551
 dorsal root, *see also* Ganglion, dorsal root. 130, 132
 general aspects, 63–64, 127, 139–152, 232–234, 236, 455, 460, 587, 640
 gray matter, 128, 130
 lateral horn, 130, 132, 149
 lumbar, 63, 146–147, 560, 566
 of nontetrapods, 139–145
 sacral, 63, 147, 559–560
 segmentation, 127
 of tetrapods, 145–152
 thoracic, 63, 560, 566
 ventral horn, 140, 148–150, 461
 ventral root, 128, 130, 149–150
 weight, 109
 white matter, 128, 130
 Spiny anteater, *see* Echidnas
 Spiracle, 159–160
 Splanchnocranium, *see* Arches, visceral
 Spot, anterior pigment, 648
Squalus, 75, 77, 291, 316–317, 352, 374, 392, 410, 420, 473, 496, 612
 Squamata, term, *see also* Lizards and Snakes. 79–80, 86
 Squid, *see* Mollusca/s, cephalopods
 Squirrels, 325, 557, 560, 566
 Stains, *see also* Neuronal tracing techniques.
 Bielschowski, 29
 Cajal, 29
 de Olmos, 29
 Fink-Heimer, 28–29
 Golgi, 28–29
 immunohistochemical, 29
 Marchi, 29
 Nauta-Gygax, 28–29
 Nissl, 29
 silver impregnation, 28–29
 Starfishes, *see* Echinodermata/es
 Starlings, 586
 Statocyst, 645
Stegosaurus, 102
 Steida, L., 69
 Stereocilia, 32
 Stomodeum, 51
 Strausfeld, N., 641
Streptopelia, 344
 Striatopallidal complex(es) (basal ganglia), general listing:
 dorsal, 328, 365, 471, 477, 480, 482–483, 489, 548
 general aspects, 60, 66, 68–69, 297, 343, 362, 364–365, 375, 397, 412, 430, 438, 471–472, 479, 484, 487, 489, 513, 540, 548–549, 551, 555, 558–560, 564, 566, 656–657
 ventral, 365, 471–472, 482, 487, 489
 Striatum, *see also* Striatopallidal complex(es).
 dorsal:
 of anamniotes, 352, 354, 418, 427, 472–477, 488, 603
 of birds:
 general aspects (lateral and medial striatum), 301, 345, 363, 369, 426, 432, 484–487, 540, 565, 584–585
 mediale, pars magnocellularis (of parrots), 345
 general aspects, 297, 334, 364, 410–411, 432, 437, 439, 472, 474, 477, 499, 509, 511–512, 611, 653, 655, 657–658
 of mammals, *see also* Nucleus, caudate-putamen. 300, 355, 359, 365, 420, 430–432, 435, 471, 477–480, 483, 487, 618, 623
 of reptiles:
 general listing, 301, 329, 426, 432, 484, 626
 of turtles, 368–369, 484
 ventral, *see also* Nucleus, accumbens and Tubercle, olfactory.
 of anamniotes, 433, 474, 575–576, 583
 of birds, 368–369, 487
 general aspects, 297, 364, 600
 of mammals, 300, 365, 430, 471, 478, 483, 487, 620
 of reptiles, 368, 484
 Striedter, G. F., 118
 Striosome/matrix organization, of dorsal striatum (of cats and monkeys), 479
 Sturgeons, *see* Chondrostei
 Subiculum, *see* Cortex, subicular
 Subpallium:
 central (of lungfishes), 595
 general aspects, 343–344, 350, 353, 432, 471, 488–489, 496, 614, 628, 657
 medial (of lungfishes), 628
 term, 66
 Subplate, 56–57, 356, 504
 Subpretectal complex (of birds), *see* Nucleus, subpretectalis and Nucleus, interstitio-pretectalis-subpretectalis
 Substance P, 25, 142, 301, 303, 462, 471–474, 476–477, 480–482, 484–487, 489, 552, 586
 Substantia:
 gelatinosa, 148
 innominata, 297, 365–367, 369, 411–412, 474, 477–478, 487, 629
 nigra:
 of amniotes, general aspects: 230, 234, 268–269, 271, 273, 282, 284, 289, 292–297, 299–303, 344, 364, 384, 425, 435–438, 478, 548, 657
 of cartilaginous fishes, 291–295, 297, 344, 489
 pars compacta:
 of birds, 268, 271, 282, 302–303, 484–485
 general aspects, 273, 292, 296, 303
 of mammals, 233, 273, 284, 297, 300–301, 303, 411–412, 478–481, 483, 487, 510, 623
 of reptiles, 484, 303
 pars reticulata,
 of birds, 268, 271, 282, 302, 387, 485–487
 general aspects, 273, 292, 296
 of mammals, 233, 297, 300, 326, 429, 435, 478–483, 487
 of reptiles, 328, 484
 Subthalamus, *see* Thalamus, ventral
 Suga, N., 414, 578
 Sulcus/i:
 calcarine, 357, 532
 central, of Rolando, 356–357, 554, 558
 collateral, 621
 development of, 356
 lateral, of Sylvius, 356–357, 532, 554, 577
 rhinal, 355, 357, 360, 366, 502, 511, 619
 term, 66, 356
 Sullivan, J., 75
 Sunfish, *see* *Lepomis*
 Superior, term, 666–667
 Surface:
 abluminal, 54
 abneural, 644

- luminal, 54
- neural, 644
- Swanson, L. W., 119, 359, 657
- Swimming, *see* Behavior, rhythmic
- Sympathetic nervous system: *see* Autonomic nervous system, sympathetic
- Synapses:
 - chemical, 23–24
 - electrical, 26
 - reciprocal, 600
- Synapsid/s, *see also* Mammals. 80–82, 96, 234, 419, 510, 524–525, 656
- Synaptic vesicles, *see* Vesicle(s), synaptic
- Syngenogue(s), term, 13
- Syngeny, *see* Homology, generative
- Syrinx, 582–583, 586, 589
- Tachyglossus*, *see also* Echidnas. 84, 357
- Tail, 43
- Takifugu*, 140
- Tanycytes, *see* Cell(s), Tanycytes
- Tape worms, 639
- Tarsirs, 528
- Taste:
 - bud, *see* Receptor, gustatory
 - general aspects,
- Taxon, term, 3
- Tectum:
 - of *Branchiostoma*, 647
 - midbrain, general organization, *see also* Colliculus, inferior, Torus, longitudinalis, *and* Torus, semicircularis. 133, 232, 267–274
- optic:
 - of amphibians, 278, 294, 312–313, 319–321, 349, 377, 422, 427, 433, 474, 476
 - of birds, 256, 271, 282–283, 302, 313, 329–333, 335, 363, 387–388, 390–391, 395–396, 428, 431, 480, 508–509, 559, 563
 - of cartilaginous fishes, 279, 291, 296, 316–317, 322–323, 334, 374, 378, 392, 420, 498–499
 - general aspects, 50, 52, 64–65, 67–69, 180, 256, 267–271, 273–274, 289–296, 298, 301–302, 304, 311–335, 344, 347, 350, 361, 375, 437, 533, 540, 653, 657
 - of hagfishes, 279, 295, 321, 334, 378
 - of lampreys, 270, 276, 290, 304, 315–317, 334, 407, 605, 612
 - of lungfishes, 277, 293, 455
 - of mammals (superior colliculus) 68, 256, 269, 274, 283, 299–300, 306, 311, 313–314, 325–328, 333, 335, 351, 355–356, 384–385, 388, 395, 408, 425, 429–430, 435–437, 459, 478, 480, 508–509, 533, 536–537, 548–550, 552–553, 559–562, 564, 566
 - of ray-finned fishes, 64–65, 216, 238, 244, 247–248, 258, 276, 279, 292–293, 298, 312, 315–319, 322–325, 334, 344, 349, 376, 379–381, 397–398, 409, 413, 421, 423, 605
 - of reptiles, 188, 268, 270, 283, 301, 312–313, 327–331, 335, 362, 386, 388, 427, 431, 480, 484, 508–509, 559, 563
 - somatosensory-multisensory, 550, 563, 566, 559
- Tegmentum, 50, 52, 64, 212, 232, 267, 269–271, 273, 277, 289–303, 357, 408, 450–451, 455, 653
- Tela choroidea, 67
- Telencephalon:
 - development of, 56–59
- general aspects, 50, 52, 64–69, 104, 164, 268–269, 273, 312, 343–344, 352, 356, 362, 397–399, 408, 418, 427, 430, 434, 471, 495–516, 645, 648–649, 651–653, 658
- Teleosts, term, *see also* Actinopterygians, teleosts; Osteoglossomorpha; Elopomorpha; *and* Clupeomorpha. 76–78, 88–89, 137, 380–383, 391–399, 413, 446, 448, 453, 592, 598–600, 605–606, 593
- Temperature, regulation, *see* Behavior, temperature regulation
- ten Donkelaar, H. J., 118, 224
- Tenrecs, 557
- Terms, *see* Nomenclature
- Territorial defense, *see* Behavior, territorial defense
- Testes, 447, 449–450
- Testosterone, 450, 457
- Tetrapods/a:
 - locomotion, 137
 - term, 73, 76, 79, 81, 86, 131, 374, 593–594, 601, 606
- Thalamus:
 - dorsal:
 - of amphibians, 418, 422, 427, 432–434
 - of birds, 419–420, 428, 431–432, 436
 - of cartilaginous fishes, 418, 420, 422–423, 430, 432, 434
 - definition, 439
 - divisions:
 - collothalamus, 120, 212, 347, 350, 361, 417–432, 436–439, 472, 474, 476, 480, 495, 501–502, 504–505, 509, 511, 514, 523, 536–537, 540, 616, 653, 655–658
 - lemnothalamus: 120, 347, 350, 361, 417–419, 432–439, 501, 505, 509–510, 514, 523–536, 538–540, 653, 655–656, 658
 - dorsal tier nuclei, 548
 - general aspects, 65–66, 68–69, 180, 212, 232, 233, 236, 269, 343, 346–347, 375, 378, 390–391, 396, 399, 407–410, 417–439, 478, 495, 497, 499, 508–510, 514, 611–612, 621, 653, 655
 - of hagfishes, 418, 422, 434
 - of lampreys, 418, 420, 432
 - limbic, 457
 - of lungfishes, 432
 - of mammals, 300, 355, 360, 365–366, 419–420, 424–425, 429–431, 434–436
 - motor, 435
 - of ray-finned fishes, 298, 350, 418, 420–423, 427, 430, 432, 434
 - of reptiles, 351, 419–420, 426–427, 431–432, 436
 - ventral tier nuclei, 548
 - ventrobasal complex, *see* Nuclear group (of dorsal thalamus of mammals), ventral
- ventral:
 - of amphibians, 350
 - of birds, 350, 352, 479, 485–487
 - of fishes, 292, 350, 605
 - general aspects, 65–66, 269, 343, 347, 350, 394, 408–409, 432, 439, 472, 478, 548, 613, 653
 - of mammals, 300, 350–351, 355, 478–483
 - of reptiles, 350–351, 479, 484
- Thecodontia/s, term, *see also* Birds, Crocodiles, *and* Dinosaurs. 80, 86
- Theory, *see also* Hypothesis.
 - Darwin-Wallace, *see* Evolution, Darwin-Wallace theory
 - neurobiotaxis, 115
 - neuromeric, 53

- parcellation, 117, 283, 485, 657
 triune brain, 114, 630
 Therian, term, 86
 Theriodonts, 525
 Therocephalians, 525
 Thireau, M., 104
 Thyroid, 447
 Tigers, 137
 Toads, *see* Anurans
 Tömböl, T., 513
 Tongue, 38–40, 137, 232, 582, 587–588, 604
 Topographic organization, *see* Organization, topographic
 Torpedo, 41, 144
 Torres, B., 216
 Torus:
 lateralis (of ray-finned fishes), 193–194, 269, 273, 276, 289, 292–293, 298, 304, 398
 longitudinalis (of ray-finned fishes), 242, 247, 257–258, 269, 274, 276, 289, 292–293, 298, 318–319, 323–325, 334, 379, 397
 semicircularis:
 electrosensory, 197, 259, 305
 general aspects, 68, 195, 197, 211–212, 260, 267, 269–270, 273–274, 276, 289–294, 298, 301, 304–306, 314, 316–318, 321, 323–325, 375, 397–398, 418, 420, 436–437, 455–456, 509–510, 575, 581
 Tracing techniques, *see* Neuronal tracing techniques
 Tract(s)/us, *see also* Bundle(s) and Pathway(s).
 alvear path, 620
 alveus, 618–620
 brachium conjunctivum, 268–269, 271–273, 279, 281, 290–291, 296–298
 central tegmental, 232–233
 cerebellospinal, 147–148, 151, 261–262
 corticobulbar, 221, 289, 558–561, 566, 580
 corticopontine, 272–273, 289
 corticothalamic, 69
 corticospinal (pyramidal):
 of birds, 510
 of mammals, 69, 131, 151–152, 221, 272–273, 289, 558, 560–561, 564–566, 657
 descending, of trigeminal, 295
 fimbria, 618–620
 forebrain bundles, *see* Bundle(s), forebrain
 fornix, 355, 357, 366, 457, 460, 611, 616, 618–621
 general aspects, 129
 gustatory-spinal, 144
 habenulointerpeduncular, *see* Fasciculus, retroflexus
 hypothalamospinal, 147, 152
 internal capsule, *see* Capsule, internal
 lateral lemniscus, *see* Lemniscus, lateral
 lobobulbaris, 451
 lobocerebellaris, 451
 mammillotegmental, 460
 mammillothalamic, 460
 medial lemniscus, *see* Lemniscus, medial
 of the mesencephalic nucleus of the trigeminal, 185, 227, 281
 occipitomesencephalicus, 271, 302, 511, 561, 565–566
 olfactory:
 general aspects, 593–595, 597–598, 605
 lateral, 66, 181, 366, 497, 595, 597–598, 600
 medial, 595, 597, 600
 optic, 36, 64, 68, 269, 274, 315, 321, 346–347, 350–351, 355, 366, 374, 376, 379, 382–385, 388–391, 410, 420–423, 426–428, 432, 451, 454, 458–459, 523, 526–527, 533
 pallii, 451
 perforant path, 620
 pineal, *see* Nerve, epiphyseal
 pyramidal, *see* Tract, corticospinal
 quintofrontal, 561
 reticulobulbar, 221, 230
 reticulospinal, 69, 131, 144, 151–152, 221, 268, 272, 564, 566
 rubrospinal, 69, 131, 144, 147–148, 151, 230, 261, 272, 290, 564, 566
 sacchi vasculosi, 446
 septomesencephalic, 363
 septo/palliomesecephalic, 485
 solitariospinal, 152
 spinal lemniscus, *see* Lemniscus, spinal
 spinocerebellar, 129, 131, 149–151, 256
 spinomesencephalic, 549, 551–552
 spino-olivary, 150
 spinoreticular, 131, 236, 549–552
 spinotectal, 131, 149
 spinothalamic, 131, 148–150, 548–551, 553
 stria:
 medullaris, 346, 351, 384, 409, 411–412, 424–425
 terminalis, 355, 359, 366–367, 424–425
 tectospinal, 129, 131, 144, 147, 152, 326, 566
 trigeminothalamic, 144, 151
 vestibulospinal, 69, 131, 144, 147–148, 151, 261, 564–565
 Transduction, sensory, 30
 Transverse, term, 666–667
 Tree shrews, 83, 96, 325, 527–529, 531–532, 566
 Tretjakoff, D., 224
 Tritocerebrum, 639–641, 645
 Trout, 382–383, 407, 409–410, 414, 489
 Tuatara, *see* *Sphenodon*
 Tuber cinereum, 455
 Tubercle, olfactory:
 of anamniotes, 474
 of birds, 345, 368–369, 487
 general aspects, 297
 of mammals, 358, 365–367, 471, 476, 478, 600, 620
 of reptiles, 368, 604
 Tuberculum, posterior, *see also* Preglomerular nuclear complex.
 of amphibians, 294, 377, 474, 476
 of cartilaginous fishes, 291, 296–297, 374, 378, 392, 396, 408, 473, 612–613
 general aspects, 65, 291–298, 303, 318, 325, 334, 343–344, 349, 373, 396–399, 496, 499, 655
 of hagfishes, *see* Area, lateralis of the posterior tuberculum (of hagfishes)
 of lampreys, 407
 nucleus medianus (of Cladistia), 318, 396, 496, 612
 periventricular nucleus of, 397
 of ray-finned fishes, 298, 318, 379, 396, 410, 477
 Tunicata/es, *see* Urochordata/es
Tupinambis, 301, 330, 362, 502, 624
 Turtles, 79–82, 85–86, 96, 119, 146–147, 208, 243, 246–247, 268, 270, 275, 283, 301, 303, 306, 312–313, 327–328, 332, 362, 368–369, 385–387, 409, 436, 448, 450, 484, 488, 539, 562, 579–580, 603, 606, 626, 628
Tyto, 199
 Ungulates, 559, 561, 566
 Unilateral, term, 666
 Urbilateria, 641, 644, 658
 Urochordata/es (= Tunicata, including ascidians), 73–74, 638, 644–646
 Urocortin, 448

- Urodela/es, 78–79, 87, 131, 205, 275, 283, 304, 312–313, 319–321, 335, 375, 409, 432–433, 474, 489, 498, 595, 597, 627
- Urophysis, 145
- Urotensin:
- I, 145
 - II, 145
- Uterus, 460–461
- Van Valen, L., 8, 12
- Vasoactive intestinal polypeptide (VIP), 25, 142, 450, 462, 552
- Vasopressin, 26
- Veenman, L., 437, 565
- Ventral:
- fold, developmental, *see* Fold, ventral
 - term, 61, 666–667
- Ventricles:
- cerebellar, 67
 - development of, 67
 - fourth, 67, 134–135
 - general aspects, 67
 - hypothalamic, 67
 - lateral, 67, 355
 - olfactory, 67
 - pineal, 594
 - tectal, 67, 269–271, 274, 278, 311
 - third, 67, 407
- Vertebra(e), 127–128
- Vertebrate(s):
- earliest, 73–75, 646, 649–655
 - groups, *see also* Group I, term *and* Group II, term. 73–89
 - term, 49, 73–75, 638, 646
- Vesalius, A., 618
- Vesicle(s):
- cerebral (*of Branchiostoma*), 645–647, 649
 - sensory (*of ascidian*), 646
 - synaptic, 21, 23–24
- Vibrissae, 43–45, 184, 555–556
- Viscera, 445, 461
- Visceromotor system, 551
- Vision/Visual:
- acuity, 529
 - belt, 541
 - binocular, 524–528
 - color, 533–534
 - contrast, 530
 - field, 534
 - frontal, evolution of, 524–526
 - monocular, 526–527
 - motion, 530
 - panoramic, 526–527
 - stereoscopic, 524, 526
 - streams, 534–536
- Vocal control pathways, *see* Pathways, vocal control
- Vocalization, *see* Behavior, vocalization *and* Behavior, learning, vocal
- Vocal learning, *see* Behavior, learning, vocal
- Volume transmission, 26
- Vomeronasal:
- amygdala:
 - nucleus sphericus, *see* Amygdala, nucleus, sphericus
 - medial nucleus, *see* Amygdala, nucleus, medial
 - general aspects, 457, 488, 504, 511, 601, 605
 - nerve, *see* Nerve, cranial, vomeronasal
 - organ, *see* Organ, vomeronasal
- von Baerian recapitulation, 60
- von Baer, K., 60, 121
- von Economo, C., 532
- Wada, H., 646
- Wada, S., 646
- Wagner, G. P., 10–12
- Wakefulness, 109, 233–234, 436, 448
- Walker, M. M., 188
- Wallabies, 555–556, 560
- Wallace, A. R., 3, 113
- Walruses, 138
- Wang, Y.-C., 542
- Waves:
- pressure, 32
 - sound, 32
- Wernicke, K., 587
- Wernicke's aphasia, *see* Aphasia, Wernicke's
- Whales, 27, 98, 102, 138, 237, 249, 303, 606
- Wicht, H., 118
- Wiesel, T., 533
- Wilczynski, W., 118
- Wild, J. M., 70, 188, 561, 564, 626
- Wiley, E. O., 8–9
- Williams, M. N., 188, 564
- Wilkschko, R., 188, 313
- Wilkschko, W., 188, 313
- Wings, 137
- Winslow, J. B., 618
- Wolves, 137
- Wombats, 555–556
- Woodpeckers, 205
- Worms (flat and tape), 639
- Wright, D., 258
- Wullimann, M. F., 118
- Wulst, *see also* Hyperpallium.
 - general aspects, 59–60, 119, 343, 361, 363, 388, 394, 495, 504, 510–511, 513–514, 516, 656
 - motor, 510, 560–561, 564, 566
 - somatosensory (somatosensory hyperpallium), 485–487, 507–508, 656
 - visual (visual hyperpallium), 394, 436, 507–508, 516, 540, 543, 560
- Xenomystus*, 197
- Xenopus*, 278, 304, 418
- Yunnanozoon*, 647, 650
- Zardoya, R., 82
- Zebra finch, *see* Finches
- Zebrafish, *see* *Danio*
- Zeier, H., 511
- Zona:
- incerta, 424–425, 478
 - limitans (*of diencephalon*), 454
- Zone(s):
- deep white, *of* cortex, 56
 - of* dorsal telencephalic area, *see individual listings under* Area, dorsal telencephalic (D)
 - dorsal thalamic (DTZ) (*of* birds), 437, 485, 487
 - intermediate, *of* cortex, 56
 - of* Lissauer, 148
 - marginal, *of* cortex, 56
 - subventricular, *of* cortex, 56
 - ventricular, *of* cortex, 54–57